BOSTON   UNIVERSITY

GRADUATE SCHOOL

Thesis

HYDROLYSIS OF NITROURETHANS

by

Howard Millard Curry

(B.S., Northeastern University,   1945)

submitted in partial fulfilment of the

requirements for the degree of

MASTER OF ARTS

1947

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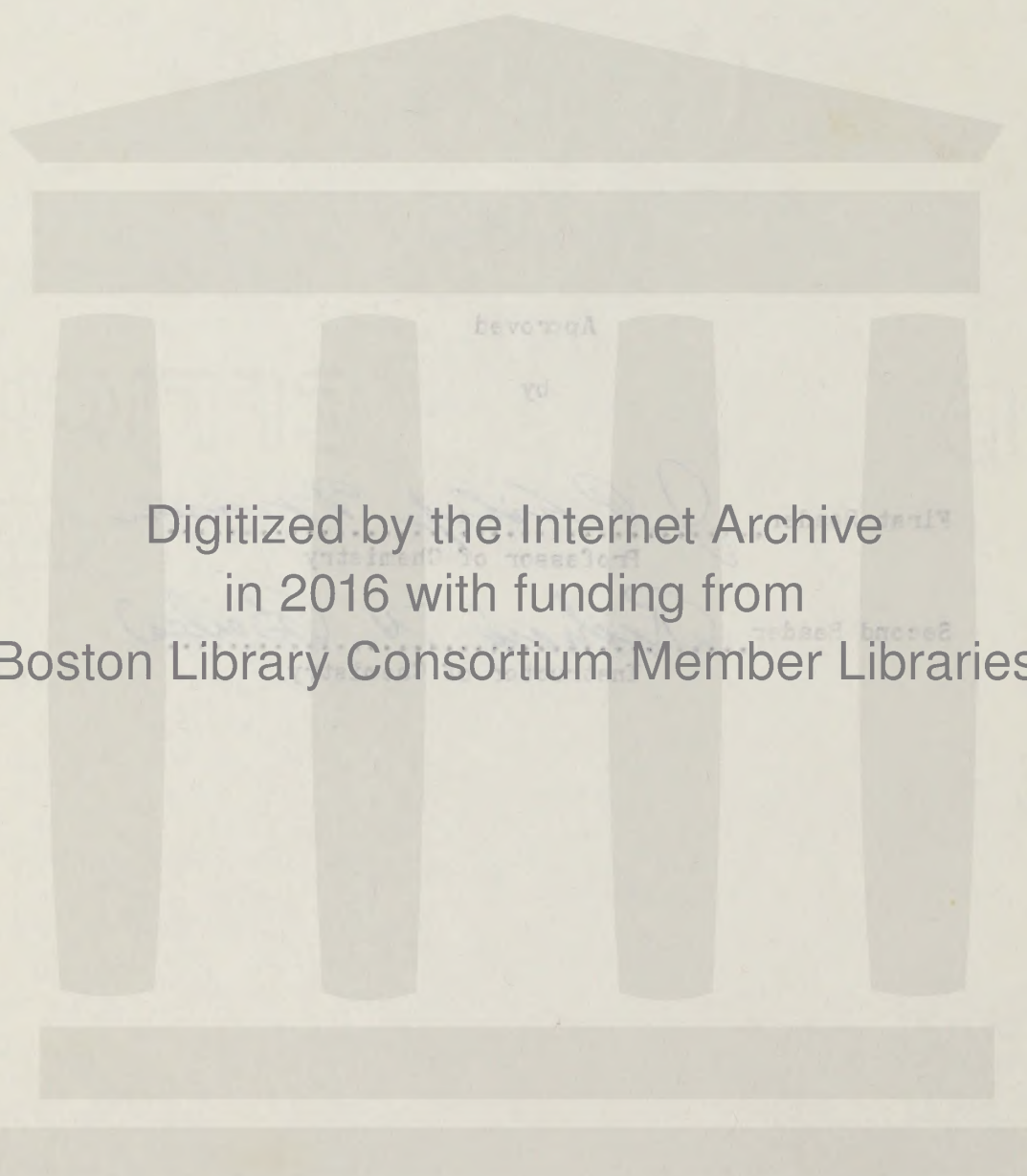
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I. INTRODUCTION

A. Historical Survey

The nitrourethans, although relatively simple in structure compared with other types of organic compounds which have been studied widely, have received very little attention from organic chemists. No more than four or five investigators have dealt with them, and then only superficially. Nitrourethans have been prepared and a few of the simpler properties determined, but at the present date the chemistry of these compounds is still in its infancy.

Probably the earliest published article on nitration of urethans was that of Thiele and Lachmann (11.) published in 1884. This nitration was performed on urethan itself by means of the following procedure:

Five-hundred cubic centimeters of pure, concentrated sulfuric acid was stirred mechanically and 100 grams of powdered urethan was added. The reaction vessel was cooled in an ice-salt bath. After all of the urethan had dissolved and the temperature had sunk below $0°C$, 110 gr. of ethyl nitrate was allowed to flow in. The cooling was so regulated that the temperature remained below $-5°C$ during the whole operation. Forty-five minutes after addition of the ethyl nitrate, the acid was poured, with stirring, onto 1.5 to 2 kg. of ice. The mixture was extracted with ether and diluted so that the total volume of the ethereal solution was about four liters.

$$C_2H_5OOC-NH_2 + C_2H_5ONO_2 \longrightarrow C_2H_5OOC-NH-NO_2 + C_2H_5OH$$

The ammonium salt was obtained from the ethereal solution by passing in a stream of dry ammonia.

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The ammonium salt was obtained from the ethereal solution by passing in a stream of dry ammonia.

$$C_2H_5OOC-NH-NO_2 \neq NH_3 \longrightarrow C_2H_5OOC-N(NH_4)-NO_2$$

The ammonium salt was then dissolved in an excess of dilute sulfuric acid and the nitrourethan was extracted with ether.

$$2C_2H_5OOC-N(NH_4)-NO_2 \neq H_2SO_4 \longrightarrow 2C_2H_5OOC-NH-NO_2 \neq (NH_4)_2SO_4$$

The ether solution was dried with calcium chloride and the ether was distilled on the water bath.

A more general method of nitrating substituted urethans was reported four years later by Franchimont and Klobbie (3.) Nitration of the substituted urethans was accomplished by means of a large excess of nitric acid. Details of their method as revised by Thomas (12.) appear later in this report. The main interest of these investigators was not directed toward the nitrourethans but to the decomposition of the former compounds by ammonia to yield nitroamines.
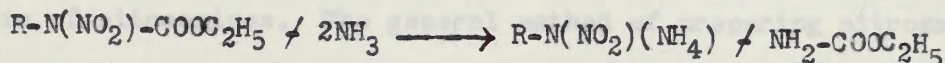
$$R-N(NO_2)-COOC_2H_5 \neq 2NH_3 \longrightarrow R-N(NO_2)(NH_4) \neq NH_2-COOC_2H_5$$

With this object in mind the following nitrourethans were prepared within the next ten years.

TABLE I

PROPERTIES OF NITROURETHANS

COMPOUND	B.P.	F.P.	Sp.gr.@ 15°C
1. Methyl ester of N-Nitro-N-n-propylcarbamic acid (12.)	139°C d.		1.187
2. Methyl ester of N-Nitro-N-isopropylcarbamic acid (12.)	120°C d.		1.1585
3. Methyl ester of N-Nitro-N-n-butylcarbamic acid (15.)		-35°C	1.149
4. Methyl ester of N-Nitro-N-sec.-butylcarbamic acid (15.)		below-70°C	1.1355

$$C_2H_5OOC-NH-NO_2 + NH_3 \longrightarrow C_2H_5OOC-N(NH_4)-NO_2$$

The ammonium salt was then dissolved in an excess of dilute sul-
furic acid and the nitrourethan was extracted with ether.

$$2C_2H_5OOC-N(NH_4)-NO_2 + H_2SO_4 \longrightarrow 2C_2H_5OOC-NH-NO_2 + (NH_4)_2SO_4$$

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TABLE I (cont.)

COMPOUND	B.P.	F.P.	Sp.gr.@ 15°C
5. Ethyl ester of N-Nitro-N-n-butylcarbamic acid (15.)		below-70°C	1.1055
6. Ethyl ester of N-Nitro-N-sec.-butylcarbamic acid (15.)		below-70°C	1.094
7. Methyl ester of N-Nitro-N-isobutylcarbamic acid (15.)		2°C	1.144
8. Ethyl ester of N-Nitro-N-isobutylcarbamic acid (15.)		below-75°C	1.101
9. Ethyl ester of N-Nitro-N-n-hexylcarbamic acid (15.)		-60°C	1.062
10. Methyl ester of N-Nitro-N-methylcarbamic acid (3.)	158°C		1.065
11. Methyl ester of N-Nitro-N-ethylcarbamic acid (3.)	165°C		1.019

The compounds listed in Table I were prepared mainly for the synthesis of nitroamines. The general method of preparing nitroamines by ammonolysis of the corresponding nitrourethans is given by Thomas (12.).

The nitrourethan was dissolved in ether and a current of dry ammonia was passed into the solution. The ammonium salt of the nitroamine precipitated as a mass of crystals, which were filtered and washed with ether.

The compound of ammonia with the nitroamine separated as a gelatinous mass which absorbed much ether and was consequently very difficult to purify. Replacing ether with either chloroform or benzene gave no better results.

The ammonium salt of the nitroamine was then decomposed with dilute sulfuric acid and the nitroamine was extracted with ether. Evaporation of the ether yielded pure nitroamines as shown by analysis.

3.

TABLE I (cont.)

COMPOUND	B.P.	M.P.	Sp.gr. a 15°
5. Ethyl ester of N-Nitro-N-n-butylcarbamic acid (15.)	below-70°C		1.1055
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10. Methyl ester of N-Nitro-N-methylcarbamic acid (3.)		158°C	1.065
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results.

The ammonium salt of the nitrosamine was then decomposed with
dilute sulfuric acid and the nitrosamine was extracted with ether.
Evaporation of the ether yielded pure nitrosamine as shown by analysis.

The nitroamines prepared by this method and their physical properties are listed in Table II.

TABLE II

PROPERTIES OF NITROAMINES

COMPOUND	B.P.	F.P.	Sp.gr.@ 15°C
1. N-Nitromethylamine (1.)		38°C	
2. N-Nitroethylamine (14.)		6°C	1.1675
3. N-Nitro-n-propylamine (12.)	128°-129°C @ 40mm.		1.102
4. N-Nitro-isopropylamine (12.)	90°-91°C @ 10mm.	-4°C	1.098
5. N-Nitro-n-butylamine (15.)		-5° to +5°C	1.0665
6. N-Nitro-sec.-butylamine (15.)		-34.5°C	1.066
7. N-Nitroisobutylamine (15.)		32.2°C	
8. N-Nitro-n-hexylamine (15.)		5.5 to 6.5°C	1.014

A great deal of work has been done with the nitroamines, especially in relation to alkyl derivatives and metallic salts of these compounds. Since one of the objects of this thesis is to characterize the hydrolysis products of nitrourethans a brief discussion of the chemistry of the nitroamines will not be out of place at this point.

Van Erp (15.) prepared the potassium salt of N-Nitro-N-n-butyl amine by mixing alcoholic solutions of the nitroamine and potassium hydroxide in equivalent quantities.

$$n\text{-}C_4H_9\text{-}NH\text{-}NO_2 + KOH \longrightarrow \left[n\text{-}C_4H_9\text{-}N\text{-}NO_2\right]^- K^+ + HOH$$

In this same paper Van Erp (15.) describes the preparation of the methyl derivative of n-butylnitroamine from equivalent quantities of the potassium salt of the nitroamine and methyl iodide in methanol solution.

$$\left[n\text{-}C_4H_9\text{-}N\text{-}NO_2\right]^- K^+ + CH_3I \longrightarrow (n\text{-}C_4H_9)(CH_3)N\text{-}NO_2 + KI$$

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3. N-Nitro-n-propylamine(12.)	128°-129°C @ 40mm.		1.102
4. N-Nitro-isopropylamine (12.)	90°-91°C @ 10mm.	-4°C	1.038
5. N-Nitro-n-butylamine (15.)		-5° to 45°C	1.0665
6. N-Nitro-sec.-butylamine (15.)		-34.5°C	1.068
7. N-Nitroisobutylamine (15.)		32.2°C	
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The work of Van Erp described above provoked a series of invest-
igations on metallic and alkyl derivatives of nitroamines by Franchimont and
his collaborators (4, 5, 13, 14). The potassium salts of ethyl and propyl-
nitroamine were prepared and other metallic derivatives were obtained from
them by reaction with various metallic salts. The sodium derivative was
obtained by reaction with alcoholic sodium hydroxide, the lithium derivative
from alcoholic lithium carbonate and the silver derivative from alcoholic
silver nitrate.

The dialkyl nitroamines, prepared by these investigators by the
reaction of an alkyl iodide with the sodium or potassium salt of a nitro-
amine, are summarized in the following table.

TABLE III

PROPERTIES OF DIALKYLNITROAMINES

COMPOUND	B.P.	Sp.gr. @ 15°C
1. N-Nitromethylethylamine (14.)	90.5°C @ 23mm.	1.1012
2. N-Nitrodiethylamine (14.)	96°C @ 18mm.	1.057
3. N-Nitro-n-propylethylamine (13.)	108°C @ 22mm.	1.028
4. N-Nitroisopropylethylamine (13.)	65°C @ 20mm.	.9783
5. N-Nitroisopropylmethylamine (13.)	51°C @ 18mm.	1.012
6. N-Nitroallylmethylamine (4.)	96°C @ 18mm.	1.1015
7. N-Nitrooctylmethylamine (5.)	164.5°C @ 17.5mm.	.965
8. N-Nitro-n-butylmethylamine (1.)		1.0268
9. N-Nitroisobutylmethylamine (1.)	104°C @ 17mm.	

B. Present Work

The foregoing historical survey of the literature reveals that
a great deal of constructive work is yet to be done on the aliphatic

The work of Van Dyk described above provoked a series of investigations on metallic and alkyl derivatives of nitrosamines by Franchimont and his collaborators (4, 5, 13, 14). The potassium salts of ethyl and propyl-nitrosamine were prepared and other metallic derivatives were obtained from them by reaction with various metallic salts. The sodium derivative was obtained by reaction with alcoholic sodium hydroxide, the lithium derivative from alcoholic lithium carbonate and the silver derivative from alcoholic silver nitrate.

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PROPERTIES OF DIALKYLNITROSAMINES

COMPOUND	B.P.	Sp.gr. @ 15°C
1. N-Nitrosdimethylamine (14.)	90.5°C @ 23mm.	1.1012
2. N-Nitrodiethylamine (14.)	96°C @ 18mm.	1.057
3. N-Nitro-n-propylamine (13.)	108°C @ 22mm.	1.038
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7. N-Nitrodiethylamine (5.)	164.5°C @ 17.5mm.	.965
8. N-Nitro-n-butylamine (1.)		1.0258
9. N-Nitrosisobutylamine (1.)	104°C @ 17mm.	

B. Present Work

The foregoing historical survey of the literature reveals that a great deal of constructive work is yet to be done on the aliphatic

nitroamines and nitrourethans. The problem of the present work consists

essentially of an attempt to determine the resistance of the nitrourethans

to hydrolysis in acidic and basic media and the concentrations of these

reagents necessary to effect complete hydrolysis in a particular interval

of time. The mechanism of the hydrolysis and the products of the hydrolysis

were to be investigated and the reaction products were to be characterized

in the event that any unfamiliar products were obtained. The experiments

described below were confined solely to one member of the nitrourethan

series, N-Nitroisopropylurethan.

Base catalyzed hydrolysis was expected to conform to the following

electronic interpretation. The first step involves attachment of the

hydroxyl group to the carbonyl carbon atom.

1. $\quad R-\overset{NO_2}{\underset{\cdot\cdot}{N}}:\overset{:\overset{\cdot\cdot}{O}:}{C}:\overset{\cdot\cdot}{O}:C_2H_5 \neq :\overset{\cdot\cdot}{O}:H \longrightarrow \left[R:\overset{NO_2}{\underset{\cdot\cdot}{N}}:\overset{:\overset{\cdot\cdot}{O}:}{\underset{:\overset{\cdot\cdot}{O}:H}{C}}:\overset{\cdot\cdot}{O}:C_2H_5 \right]^-$
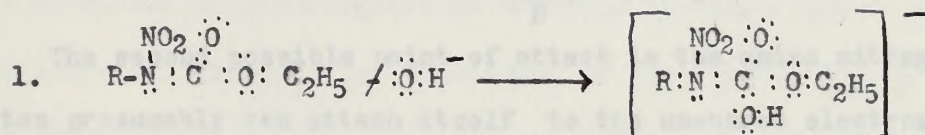
The resulting negative ion then reacts with the water in the reaction

medium.

2. $\quad \left[R:\overset{NO_2}{\underset{\cdot\cdot}{N}}:\overset{:\overset{\cdot\cdot}{O}:}{\underset{:\overset{\cdot\cdot}{O}:H}{C}}:\overset{\cdot\cdot}{O}:C_2H_5 \right]^- \neq H:\overset{\cdot\cdot}{O}:H \longrightarrow R:\overset{NO_2}{\underset{\cdot\cdot}{N}}:\overset{:\overset{\cdot\cdot}{O}}{\underset{:\overset{\cdot\cdot}{O}:H}{C}} \neq C_2H_5:\overset{\cdot\cdot}{O}:H \neq :\overset{\cdot\cdot}{O}:H^-$
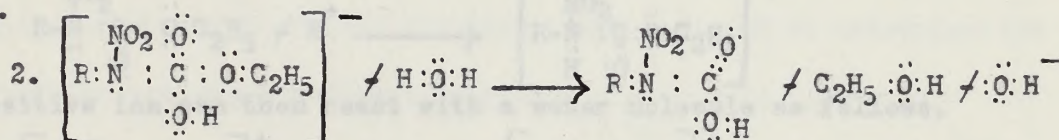
Thus we see that the molecule is split and the catalyst is regenerated.

The last step involves decomposition of the unstable carbamic acid type of

compound to yield carbon dioxide and a nitroamine.

3. $\quad R:\overset{NO_2}{\underset{\cdot\cdot}{N}}:\overset{:\overset{\cdot\cdot}{O}}{C}:\overset{\cdot\cdot}{O}:H \longrightarrow R-\overset{NO_2}{\underset{\cdot\cdot}{N}}-H \neq CO_2$
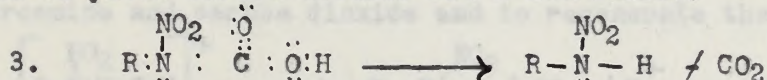
If hydrolysis is effected in an acid medium, there are two points

in the nitrourethan molecule which might be attacked by the reagent. The

carbonyl oxygen atom can assume a negative charge through resonance.

$$R-\overset{NO_2}{\underset{\cdot\cdot}{N}}-\overset{:\overset{\cdot\cdot}{O}:^-}{\underset{+}{C}}:\overset{\cdot\cdot}{O}:R^1 \longleftrightarrow R-\overset{NO_2}{\underset{\cdot\cdot}{N}}-\overset{O}{C}{'}-OR^1$$
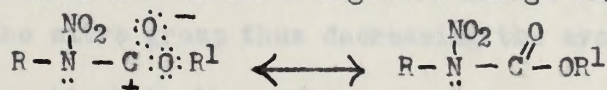
   If hydrolysis actually followed a path similar to that of ester hydrolysis, the mechanism would be as follows.

   The first step would involve the attack of a proton upon the carbonyl oxygen atom.

1. $R\underset{\cdot\cdot}{\overset{NO_2}{N}}:\overset{O}{C}-OR' \not H^+ \longrightarrow R-\overset{NO_2}{\underset{\cdot\cdot}{N}}-\overset{\overset{+}{OH}}{C}-OR'$ or $R\overset{NO_2}{\underset{\cdot\cdot}{N}}-\overset{OH}{\underset{+}{C}}-OR'$
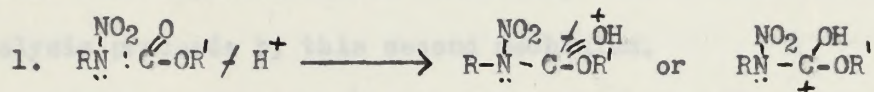
The resulting positive ion can then react with a molecule of water, decomposing the ion and regenerating the catalyst.

2. $R-\overset{NO_2}{\underset{+}{N}}-\overset{OH}{C}-OR^1 \not H:\overset{\cdot\cdot}{O}:H \longrightarrow R-\overset{NO_2}{\underset{\cdot\cdot}{N}}-\overset{O}{\underset{OH}{C}} \not R^1OH \not H^+$
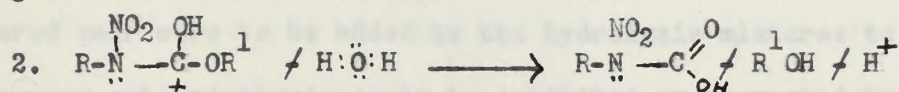
Again the unstable carbamic acid derivative should decompose to give the nitroamine and carbon dioxide.

3. $R-\overset{NO_2}{\underset{\cdot\cdot}{N}}-\overset{O}{C}-OH \longrightarrow R-\overset{NO_2}{N\underset{H}{\diagdown}} \not CO_2$
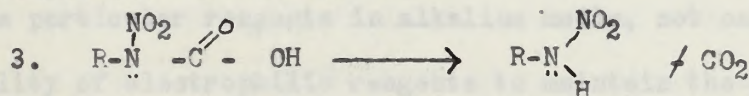
   The second possible point of attack is the amino nitrogen atom. The proton presumably can attach itself to the unshared electron pair at this point.

1. $R-\overset{NO_2}{\underset{\cdot\cdot}{N}}:\overset{\cdot\cdot}{\underset{\cdot\cdot}{C}}:\overset{\cdot\cdot}{O}:C_2H_5 \not H^+ \longrightarrow \left[R-\overset{NO_2}{\underset{H}{N}}:\overset{\cdot\cdot}{\underset{:\overset{\cdot\cdot}{O}}{C}}:\overset{\cdot\cdot}{O}:C_2H_5 \right]^+$
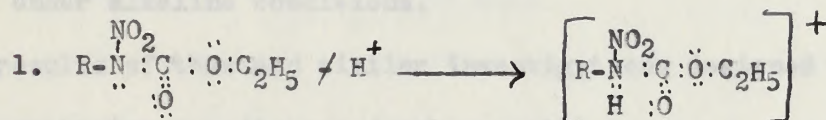
This positive ion can then react with a water molecule as follows.

2. $\left[R-\overset{NO_2}{\underset{H}{N}}:\overset{\cdot\cdot}{\underset{:\overset{\cdot\cdot}{O}}{C}}:\overset{\cdot\cdot}{O}:C_2H_5 \right]^+ \not H:\overset{\cdot\cdot}{O}:H \longrightarrow \left[R-\overset{NO_2}{\underset{H}{N}}:\overset{\cdot\cdot}{\underset{:\overset{\cdot\cdot}{O}}{C}}:\overset{\cdot\cdot}{O}:H \right]^+ \not H:\overset{\cdot\cdot}{O}:C_2H_5$
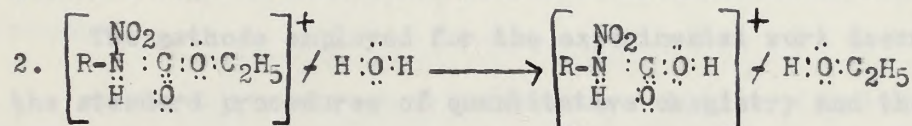
The resulting carbamic acid type of compound will then decompose to yield the nitroamine and carbon dioxide and to regenerate the catalyst.

3. $\left[R-\overset{NO_2}{\underset{H}{N}}:\overset{\cdot\cdot}{\underset{:\overset{\cdot\cdot}{O}}{C}}:\overset{\cdot\cdot}{O}:H \right]^+ \longrightarrow R-\overset{NO_2}{N\underset{H}{\diagdown}} \not CO_2 \not H^+$
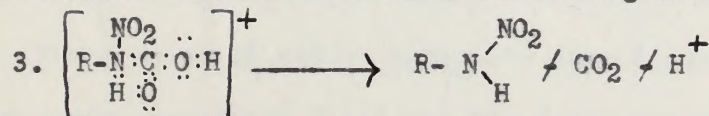
There is, however, a possibility that hydrolysis cannot proceed by this second postulated mechanism because the unshared pair of electrons can resonate with the nitro group thus decreasing the availability of this unshared pair to attack by the proton.

$$\overset{\cdot\cdot}{\underset{\cdot\cdot}{O}}:\overset{+}{N}:\overset{\cdot\cdot}{O}^{-} \qquad \overset{-}{O}-\overset{+}{N}-O^{-} \qquad \overset{O}{\underset{+}{N}}\overset{+}{-}O^{-}$$
$$R\overset{\cdot\cdot}{-}\overset{\cdot\cdot}{N}-C\overset{\curvearrowleft O}{-}OR \qquad R-\overset{+}{\underset{+}{N}}-C\overset{\curvearrowleft O}{-}OR \qquad R-\overset{+}{\underset{+}{N}}=C\overset{O^{-}}{-}OR$$
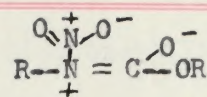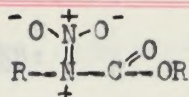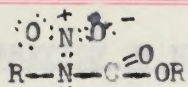
Structures of this type, especially since some of them place a negative charge on the carbonyl oxygen atom, a requisite for proton attachment in the first postulated mechanism, make it seem rather doubtful that hydrolysis proceeds by this second mechanism.

Reasoning on the basis of the second mechanism certain electrophilic reagents and reagents capable of forming a hydrogen bond with the unshared pair were to be added to the hydrolysis mixtures to determine whether or not hydrolysis could be inhibited or prevented by their presence.

It was also postulated that hydrolysis could not be prevented by these particular reagents in alkaline media, not only because of the inability of electrophilic reagents to maintain the open sextet in basic solution which is necessary for attachment of the inhibitor to the unshared electron pair; but also hydrolysis was expected to proceed by a different path under alkaline conditions.
The results of this and similar investigations designed to determine the true mechanism are discussed subsequently.

The methods employed for the experimental work described below were the standard procedures of quantitative chemistry and the preparative techniques of the organic chemist.

II PREPARATION OF NITROURETHANS:

Nitrourethans were first investigated and employed for the synthesis of nitroamines by Franchimont and Klobbie (3.). Their method of preparation as revised by Thomas (12.) is described briefly in the following paragraphs.

Either ethyl or methyl chloroformate was cooled in an ice bath and a 25% aqueous solution of the amine was added slowly. The product was extracted with ether and the ethereal solution was dried and fractionally distilled. The urethans obtained in this manner were nitrated as follows: The urethans were added drop by drop to 3 or 4 molecular equivalents of nitric acid, keeping the temperature at about 0°C. The nitric acid solution was then poured onto crystals of sodium carbonate which were covered with a little water and the whole mixture was cooled. A yellowish liquid separated and was extracted with ether. The ether was distilled and the residue was dried by extraction with sulfuric acid.

The isopropyl nitrourethan used in this research was prepared by the same basic procedure as that outlined above but many improvements have been added.

A two-liter three-necked flask was used, equipped with a 500 c.c. dropping funnel, a mechanical stirrer and a thermometer. The compound used in these researches was always prepared in batches of the following size: Three moles of sodium hydroxide were dissolved in 180-210 c.c. of wwater in the two-liter flask and the flask was cooled in an ice-bath. Three moles of isopropylamine in 90 c.c. of water were added slowly with stirring, keeping the temperature of the reaction mixture at about 0°C. Then three moles of ethylchlorocarbonate were added through the dropping

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funnel at such a rate that the temperature did not rise above 15°C. A 5% excess of the amine was used. After complete addition of the ethyl chlorocarbonate (about 2 hours), stirring was continued for about fifteen minutes. Then the mixture was placed in a separatory funnel and the bottom layer was drawn off. The top layer was dried with the least possible quantity of potassium carbonate so that it appeared clear, not turbid. The isopropylurethan was then distilled under reduced pressure using a water pump (B.P. 64°C @ 7mm). The low boiling fraction was isopropylamine.

The reaction proceeds as shown by the following equation.

$$C_2H_5-O-\overset{O}{\overset{\|}{C}}-Cl + H_2N-CH(CH_3)_2 + NaOH \longrightarrow (CH_3)_2-CH-\overset{H}{N}-\overset{O}{\overset{\|}{C}}-O-C_2H_5 + NaCl + H_2O$$
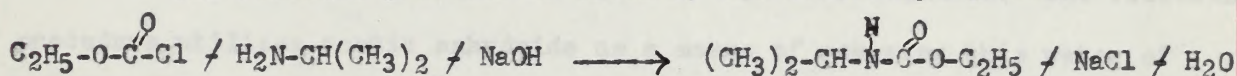
The quantities of reagents employed in this preparation were based on the following calculations:

1. $CH_3-CH_2O\overset{O}{\overset{\|}{C}}-Cl$, M.W. = 109, 3 x 109 = 327gr.

2. $(CH_3)_2-CH-NH_2$, M.W. = 60, 3 x 60 = 180gr.

5% excess (180)(105/100) = 189   189gr.

3. NaOH, M.W. = 40. 3 x 40 = 120

Assuming that the NaOH is 90% pure: (120)(100/90) = 133

For safety a 10% excess is used: (133)(110/100) = 147   147gr.

Function of the sodium hydroxide:

The reaction may be carried out in the absence of base but under such conditions two moles of amine are required to react with one mole of the ethyl chlorocarbonate. The first mole of the amine would then react with the ethylchlorocarbonate to form the urethan and the second mole would react with the hydrogen chloride produced by the first reaction to yield the amine hydrochloride.

$$(CH_3)_2CH-NH_2 + HCl \longrightarrow (CH_3)_2CH-NH_2-HCl$$

The use of the sodium hydroxide is to neutralize this HCl as rapidly as it
is formed so that the amine may remain free for reaction with the ethyl-
chlorocarbonate.

Nitration of the isopropylurethan:

The method of Franchimont and Klobbie (3.) required three or four
times the theoretical amount of nitric acid if nitration was to be effected
satisfactorily, the main reason being that the water produced in the reaction
so diluted the nitric acid when only one molecular equivalent was used
that its efficiency as a nitrating agent was greatly impaired. The following
procedure utilizes acetic anhydride as a means of removing this water of
of reaction.

$$(CH_3CO)_2O \not{} H_2O \longrightarrow 2CH_3COOH$$

The overall reaction proceeds as follows.

$$(CH_3)_2\text{-CH-NH-C}\overset{O}{\text{-}}\text{O-C}_2H_5 \not{} HONO_2 \not{}(CH_3CO)_2O \longrightarrow (CH_3)_2\text{-CH-N}(NO_2)\text{-C}\overset{O}{\text{-}}\text{O-C}_2H_5 \not{}2CH_3COOH$$
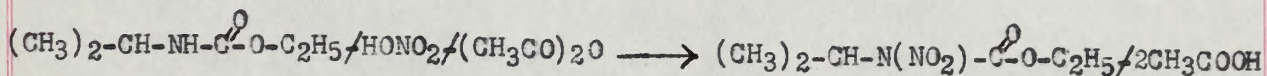
This procedure was carried out on all of the product obtained in the prev-
ious discussion. The quantities of reagents employed will be discussed
later.

Fuming nitric acid (white) was added through a dropping funnel
to the acetic anhydride which was enclosed in a two-liter, three-necked
flask which was equipped with a thermometer and a mechanical stirrer. The
flask was cooled in an ice-salt mixture and during the addition of the nitric
acid the temperature was not allowed to rise above $10^{\circ}C$, keeping it most of
the time between $5^{\circ}- 8^{\circ}C$. After the nitric acid was added, the ice bath was
replaced by a water bath at approximately $18^{\circ}C$. The urethan was then added
at such a rate that the temperature remained below $35^{\circ}C$. After all of the
urethan had been added, stirring was continued for ten minutes.

The reaction mixture was poured into a volume of water which was about three times its own volume. The nitrourethan was the bottom layer. The nitrourethan was separated and washed repeatedly with dilute potassium carbonate solution until free from acid. It was washed with water and dried by filtering through two or three pieces of filter paper. It was then distilled under reduced pressure using an electric pump.

(B.P. 72° @ 7mm) ($M_D^{20} = 1.4381$).

Discussion of Quantities used:

1. Enough acetic anhydride must be used to react with all of the water in the nitric acid and all of the water formed in the reaction.

2. The acetic anhydride used was assumed to be 90% pure. The calculations were based on this and a 5% excess was used for safety.

3. The fuming nitric acid used was 87% HNO_3.

4. For rapidity and safety a 50% excess of nitric acid was used.

Calculations:

HNO_3, M.W. = 63, 3 moles = 3x63 = 189gr.

HNO_3 (fuming) is 87% HNO_3

Therefore the weight of solution necessary to insure the presence of three moles of HNO_3 is:

(189) (100/87) = 217 grams.

It is intended, however to use a 50% excess of HNO_3, since a 50% excess is necessary for a complete nitration.

(217) (1.50) = 325 grams.

Weight of water in 325 grams of fuming nitric acid:

Since we have 87% HNO_3 we must have 13% H_2O.

(325) (.13) = 42.3 grams of water

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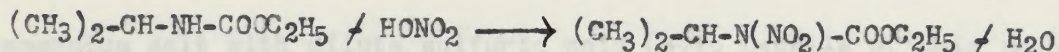
$$(42.3/18) = 2.35 \text{ moles.}$$

<u>Water of Reaction:</u>

$$(CH_3)_2\text{-}CH\text{-}NH\text{-}COOC_2H_5 + HONO_2 \longrightarrow (CH_3)_2\text{-}CH\text{-}N(NO_2)\text{-}COOC_2H_5 + H_2O$$

If three moles of urethan react, three moles of water will be formed.

<u>Total moles of water requiring removal:</u>

$$3 + 2.35 = 5.35 \text{ moles } H_2O$$

<u>Acetic Anhydride:</u>

One mole of acetic anhydride reacts with one mole of water.

$$(CH_3CO)_2O + H_2O \longrightarrow 2CH_3COOH$$

$$\text{M.W.} = 102, \quad 1 \text{ mole} = 102 \text{ grams.}$$

Weight of Acetic Anhydride necessary to react with all water.

$$(102)(5.35) = 546 \text{ grams.}$$

Since this is assumed to be only 90% $(CH_3CO)_2O$ we use:

$$(546)(100/90) = 606 \text{ grams.}$$

For safety a 5% excess of $(CH_3CO)_2O$ should be used.

$$(606)(105/100) = 636 \text{ grams}$$

<u>Summary</u>

To nitrate three moles of isopropylurethan:

393 gr. isopropylurethan

325 gr. fuming nitric acid

636 gr. acetic anhydride

Moles of water in nitric acid used:

(42.3/18) = 2.35 moles.

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$(CH_3)_2\text{-}CH\text{-}NH\text{-}COOC_2H_5$ + $HONO_2$ ──→ $(CH_3)_2\text{-}CH\text{-}N(NO_2)\text{-}COOC_2H_5$ + H_2O

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III BASIC HYDROLYSIS

A. Introduction

The classical method of decomposing a nitrourethan was to run dry
ammonia into its ethereal solution and to decompose the precipitated
ammonium salt with dilute sulfuric acid (3.). Details of this process are dis-
cussed in the introductory section of this paper.
The reaction proceeds as follows:

$$R-N(NO_2)-COOC_2H_5 \,/\, 2NH_3 \longrightarrow R-N(NO_2)(NH_4) \,/\, NH_2-COOC_2H_5$$

Search of the literature, however, revealed no attempts at bring-
ing about a similar reaction by means of hydrolysis. On the basis of the
above equation it seemed logical to conclude that hydrolysis would take
place in the following manner:

$$R-N(NO_2)-COOC_2H_5 \,/\, HOH \longrightarrow R-NH-NO_2 \,/\, HO-COOC_2H_5$$
$$HO-COO-C_2H_5 \longrightarrow C_2H_5OH \,/\, CO_2$$

Since there was no evidence of experimentation along this line by previous
investigators, instigation of a program of research along these lines ap-
peared to be desirable.

The procedure used for the hydrolysis of N-Nitroisopropylurethan
and determination of percentage hydrolysis is relatively simple and worked
well from the very first.

The compound was hydrolyzed by refluxing it for certain definite
periods of time with sodium hydroxide of varying concentrations. It was
predicted that the nitrourethan would hydrolyze in such a way that for every
mole of urethan hydrolyzed, a mole of carbon dioxide would be produced.

$$(CH_3)_2-CH-N(NO_2)-COOC_2H_5 \,/\, HOH \longrightarrow (CH_3)_2-CH-NH-(NO_2) \,/\, CO_2 / C_2H_5OH$$

The carbon dioxide would of course react with the alkaline medium thusly:

$$CO_2 \,/\, 2NaOH \longrightarrow Na_2CO_3 \,/\, H_2O$$

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The carbon dioxide would of course react with the alkaline medium thusly:

$$CO_2 + 2NaOH \longrightarrow Na_2CO_3 + H_2O$$

The work of Thomas (12.) suggested that probably the resulting nitroamine would be converted into its sodium salt.

$$(CH_3)_2CH-NH-NO_2 + NaOH \longrightarrow (CH_3)-CH-NNa-NO_2 + H_2O$$

The hydrolysis mixtures were then transferred quantitatively to volumetric flasks. Aliquot portions were then taken and titrated to the phenolphthalein end-point with dilute HCl. The following two reactions were expected.

$$NaOH + HCl \longrightarrow NaCl + H_2O$$
$$Na_2CO_3 + HCl \longrightarrow NaHCO_3 + NaCl$$

The titration was then continued to the methyl orange end-point during which time the following reaction was expected to take place.

$$NaHCO_3 + HCl \longrightarrow NaCl + CO_2 + H_2O$$

In this manner it was proposed to determine the percentage hydrolysis by quantitative titration of the carbon dioxide evolved in the reaction.

However, basing the calculations for some of the earlier runs on the above equations alone, gave results in the vicinity of 200% hydrolysis.

If we consider the products of the reaction, however, we find that the isopropylnitroamine can form a sodium derivative which cannot exist in acid solution. For every molecule of carbon dioxide formed by hydrolysis of the nitrourethan, a molecule of the nitroamine is also formed. The nitroamine would then form its sodium derivative very rapidly.

$$(CH_3)_2CH-NH-NO_2 + NaOH \longrightarrow (CH_3)_2CH-NNa-NO_2 + H_2O$$

If we assume that the sodium derivative is present at the phenolphthalein end point and is decomposed completely only at the methyl orange end point, it is obvious that we have the following two reactions contributing to the titration.

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$$NaHCO_3 + HCl \longrightarrow NaCl + CO_2 + H_2O$$

$$(CH_3)_2CH-NNa-NO_2 + HCl \longrightarrow (CH_3)_2CH-NH-NO_2 + NaCl$$

Thus it is shown that two equivalents of hydrochloric acid are necessary for every equivalent of nitrourethan hydrolyzed. It is clear that hydrolysis of the nitrourethan in basic medium proceeds as follows:

$$(CH_3)_2-CH-N(NO_2)-COOC_2H_5 + 3NaOH \longrightarrow (CH_3)_2-CH-NNa-NO_2 + Na_2CO_3 + C_2H_5OH + H_2O$$

and that three moles of sodium hydroxide are required for every mole of nitrourethan.

On the basis of the above reasoning, runs in which hydrolysis was obviously complete gave 100% hydrolysis rather than 200% upon application of the appropriate calculations.

When the isopropylnitroamine was finally isolated (see below) it was found that its water solutions were acidic to litmus and that quite a few drops of 10% NaOH solution were necessary to bring out the red color of the phenolphthalein.

B. General method of Investigation:

The hydrolyses in basic media were all carried out in this manner: A 500 c.c. round bottomed flask equipped with a long reflux condenser was used as a reaction vessel. One-hundred cubic centimeters of sodium hydroxide solution of the desired concentration were pipetted into this flask and a small quantity of isopropylnitrourethan was weighed into the flask from a small dropping bottle. A boiling chip was added and the mixture was refluxed for the desired length of time. The mixture was then allowed to cool and transferred quantitatively to a 200 c.c. volumetric flask and diluted to volume. Aliquot portions (50 c.c.) were then titrated with dilute hydrochloric acid to the phenolphthalein end point.

$$NaHCO_3 + HCl \longrightarrow NaCl + CO_2 + H_2O$$

$$(CH_3)_2C=NNa-NO_2 + HCl \longrightarrow (CH_3)_2CH-N=NO_2-OH + NaCl$$

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From this point on the titration was continued with standard hydrochloric

acid (approximately .4N) standardized against standard sodium carbonate.

Appropriate blanks were run from a solution containing 100 c.c. of the

NaOH solution and 100 c.c. of water. The percentage hydrolysis was cal-

culated from the type of data shown below:

C. Sample Calculation:

Basic Hydrolysis of N-Nitroisopropylurethan (5% NaOH)

(4 hours refluxing, 100 c.c. of 5% NaOH)

Wt. bottle and sample	47.8219
Wt. bottle	37.4822
Wt. sample	10.3397

The molecular weight of N-Nitro isopropylurethan is 176, while that of

CO_2 is 44. 176/44 = 4. The factor, 4, is used to obtain the weight of

CO_2 possible to observe by dividing it into the weight of the sample.

Thus, theoretical CO_2 10.3397/4 = 2.5849 gr.

Moles CO_2:   2.5849/44 = .05875 = 58.75 millimoles

In a 50 c.c. aliquot there will be: 58.75/4 = 14.69 millimoles

TITRATIONS

	I				II	
End	49.23	1.02		End	49.60	
Start	.58	.28		Start	.25	
Total	48.65	≠	.74		Total	49.35
Total	49.39					

Volume of HCl necessary for the blank = .60 c.c.

Average titrated volume 49.37 c.c.

49.37 - .60 = 48.77 c.c.

From this point on the titration was continued with standard hydrochloric acid (approximately .4N) standardized against standard sodium carbonate. Appropriate blanks were run from a solution containing 100 c.c. of the NaOH solution and 100 c.c. of water. The percentage hydrolysis was calculated from the type of data shown below:

c. Sample Calculation:

<u>Basic Hydrolysis of N-Nitrosomorpholurethan (5% NaOH)</u>

(4 hours refluxing, 100 c.c. of 5% NaOH)

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Wt. bottle	37.4822
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End	49.23	1.02		End	49.60
Start	.58	.28		Start	.25
Total	48.65	.74		Total	49.35
Total	49.39				

Volume of HCl necessary for the blank = .50 c.c.

Average titrated volume 49.37 c.c.

49.37 - .50 = 48.77 c.c.

If the hydrolysis were complete 14.7 millimoles of CO_2 would be titrated, but since we have an equivalent amount of nitroamine formed, the total titration should run to $2 \times 14.7 = 29.4$ millimoles:

The HCl used had a normality of .4531

$$(.4531)(48.77) = 22.1 \text{ millimoles}$$

Thus:

Percentage Hydrolysis (4 hrs.) $(100)(22.1)/29.4$ 75.2%

The results obtained by this method are tabulated below:

TABLE IV

PERCENTAGE HYDROLYSIS IN BASIC MEDIUM

% NaOH	Volume	Time	% Hydrolysis
10%	100 c.c.	4 hrs.	96.4%
10%	100 c.c.	4 hrs.	98.3%
10%	100 c.c.	3 hrs.	99.1%
10%	100 c.c.	2 hrs.	95.4%
20%	100 c.c.	4 hrs.	94.3%
5%	100 c.c.	4 hrs.	75.2%
5%	150 c.c.	6 hrs.	97.2%
3%	100 c.c.	4 hrs.	54.7%
1%	100 c.c.	4 hrs.	31.5%

In the case of the one percent hydrolysis tabulated above, the mixture was neutral to both litmus and phenolphthalein at the end of the refluxing. The value 31.5% was obtained by titration directly to the methyl orange end point.

D. Further Hydrolysis:

It was thought at the initiation of this investigation that

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30%	100 c.c.	4 hrs.	94.3%
5%	100 c.c.	4 hrs.	75.2%
5%	150 c.c.	6 hrs.	97.2%
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D. Further Hydrolysis:

It was thought at the initiation of this investigation that

further hydrolysis might occur to yield isopropyl amine and nitric acid
according to the following equation.

$$(CH_3)_2-CH-NH-NO_2 + HOH \longrightarrow (CH_3)_2-CH-NH_2 + HONO_2$$

The amine if liberated would undoubtedly escape as vapor from the hot
alkaline solution.

Its presence could not be detected by smell and moistened piece
of red lutmus paper fastened to the top of the condenser did not change
color throughout the refluxing even when 20% NaOH was employed. Attempts
to get a brown ring test with ferrous sulfate solution and concentrated
sulfuric acid on the reaction mixture were futile. We may therefore con-
clude that,at least in the hydrolysis media employed, the nitroamine does
not hydrolyze.

The nitroamine employed was extracted from the reaction mixture with ether,
the ether distilled on a steam bath and the residue distilled under reduced
pressure. It is evidently 97.0% pure.

3. Addition of Excess Alkali and Back Titration with HCl

A weighed sample of the nitroamine was dissolved in 50 c.c. of
water and an excess of standard alkali was added so the phenolphthalein
end-point was definitely past. The mixture was then titrated to both the
phenolphthalein and the methyl orange end points with standard HCl.

Weight of sample: .8200 gr.

.8200/104 = .00789 moles of nitroamine

Total volume of base added   44.84 c.c. (.260N)

(44.84) (.260) = 11.67 m.e. NaOH

Volume of acid to reach phenolphthalein end point 33.06 c.c.(.116N)

(33.06) (.116) = 3.83 m.e.

further hydrolysis might occur to yield isopropyl amine and nitric acid according to the following equation.

$$(CH_3)_2-CH-NH-NO_2 + HOH \longrightarrow (CH_3)_2-CH-NH_2 + HONO_2$$

The amine if liberated would undoubtedly escape as vapor from the hot alkaline solution.

Its presence could not be detected by smell and moistened piece of red litmus paper fastened to the top of the condenser did not change color throughout the refluxing even when 20% NaOH was employed. Attempts to get a brown ring test with ferrous sulfate solution and concentrated sulfuric acid on the reaction mixture were futile. We may therefore conclude that, at least in the hydrolysis media employed, the nitrosamine does not hydrolyze.

E. Evidence for Correctness of Analytical Procedure

    1. Neutral Equivalent of Isopropylnitroamine

        A weighed sample of isopropylnitroamine was dissolved in 50 c.c. of distilled water and titrated to the phenolphthalein end point with standard sodium hydroxide solution.

           Weight of sample: .8205 gr.

           Volume of NaOH: 29.34 c.c.

           Normality of NaOH: .260

           Molecular Weight   104

      .8205/104 = .00790 moles of nitroamine

        (29.34) (.260) = .00765 moles of NaOH

       (100) (.00765)/(.00790) = 97.0% pure.

The nitroamine employed was extracted from the reaction mixture with ether, the ether distilled on a steam bath and the residue distilled under reduced pressure. It is evidently 97.0% pure.

    2. Addition of Excess Alkali and Back Titration with HCl

        A weighed sample of the nitroamine was dissolved in 50 c.c. of water and an excess of standard alkali was added so the phenolphthalein end-point was definitely past. The mixture was then titrated to both the phenolphthalein and the methyl orange end points with standard HCl.

           Weight of sample: .8200 gr.

       .8200/104 = .00789 moles of nitroamine

    Total volume of base added   44.84 c.c. (.260N)

        (44.84) (.260) = 11.67 m.e. NaOH

   Volume of acid to reach phenolphthalein end point 33.86 c.c.(.116N)

        (33.86) (.116) = 3.92 m.e.

F. Evidence for Correctness of Analytical Procedure

1. Neutral Equivalent of Isonitrosylchromine

A weighed sample of isonitrosylchromine was dissolved in 50 c.c. of distilled water and titrated to the phenolphthalein end point with standard sodium hydroxide solution.

Weight of sample:	.8205 gr.
Volume of NaOH:	29.34 c.c.
Normality of NaOH:	.560
Molecular Weight	104

$$.8205/104 = .00790 \text{ moles of nitrosamine}$$
$$(29.34)(.560) = .00765 \text{ moles of NaOH}$$
$$(100)(.00765)/(.00790) = 97.0\% \text{ pure.}$$

The nitrosamine employed was extracted from the reaction mixture with ether, the ether distilled on a steam bath and the residue distilled under reduced pressure. It is evidently 97.0% pure.

2. Addition of Excess Alkali and Back Titration with HCl

A weighed sample of the nitrosamine was dissolved in 50 c.c. of water and an excess of standard alkali was added so the phenolphthalein end-point was definitely past. The mixture was then titrated to both the phenolphthalein and the methyl orange end points with standard HCl.

Weight of sample: .8200 gr.

$$.8200/104 = .00789 \text{ moles of nitrosamine}$$

Total volume of base added   44.84 c.c. (.260N)

$$(44.84)(.260) = 11.67 \text{ m.e. NaOH}$$

Volume of acid to reach phenolphthalein end point 33.86 c.c.(.116N)

$$(33.86)(.116) = 3.93 \text{ m.e.}$$

Millequivalents of Base Neutralized by Nitroamine:

11.67-3.92 = 7.75 = .00775 moles.

Percentage Purity of the Nitroamine:

(100) (.00775)/(.00789) = 98.2%

Volume of acid to reach methyl orange end point:66.18c.c.
(.116N)

(66.18) (.116) = 7.73 m.e. = .00773 moles.

Percentage Purity of the Nitroamine:

(100) (.00773)/(.00789) = 98.0%

3. <u>Preparation of a Mixture of Hydrolysis Products as Postulated</u>.

A mixture corresponding to the composition of a solution after hydrolysis with 10% NaOH was prepared. On the basis of a 5 gram sample of N-Nitroisopropylurethan (.0284 moles) the following quantities of reagents were employed.

7.72 gr sodium hydroxide

94 c.c. distilled water

2.96 gr. isopropylnitroamine

3.01 gr. sodium carbonate

1.30 gr. ethyl alcohol (absolute)

The mixture was diluted to a volume of 200 c.c. in a volumetric flask. A 50 c.c. aliquot portion was taken and diluted with 50 c.c. of distilled water. It was titrated with standard acid using both indicators and a pH meter. The indicator color changes corresponded with the rapid pH changes as shown by the potentiometer. The HCl used was .567 N. Figure I was constructed by plotting the measured pH against the volume of standard acid added. The calculations for determining percentage hydrolysis were applied to this mixture as follows.

Milliquivalents of Base Neutralized by Nitrosamine:

11.67-3.92 = 7.75 = .00775 moles.

Percentage Purity of the Nitrosamine:

(100)(.00775)/(.00789) = 98.2%

Volume of acid to reach methyl orange end point:66.18c.c.
(.116N)

(66.18)(.116) = 7.75 m.e. = .00773 moles.

Percentage Purity of the Nitrosamine:

(100)(.00773)/(.00789) = 98.0%

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A mixture corresponding to the composition of a solution after

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pH changes as shown by the potentiometer. The HCl used was .567 N. Figure

I was constructed by plotting the measured pH against the volume of stand-

ard acid added. The calculations for determining percentage hydrolysis

were applied to this mixture as follows.

Potentiometric Titration from the
Phenolphthalein End Point to the
Methyl Orange End Point Using a
Weighed Out Mixture of the
Composition Postulated After
Complete Hydrolysis of Five Grams
of N-Nitroisopropylurethan by 100 c.c.
of 10% NaOH.

Volume of .567N HCl

Figure I.

pH
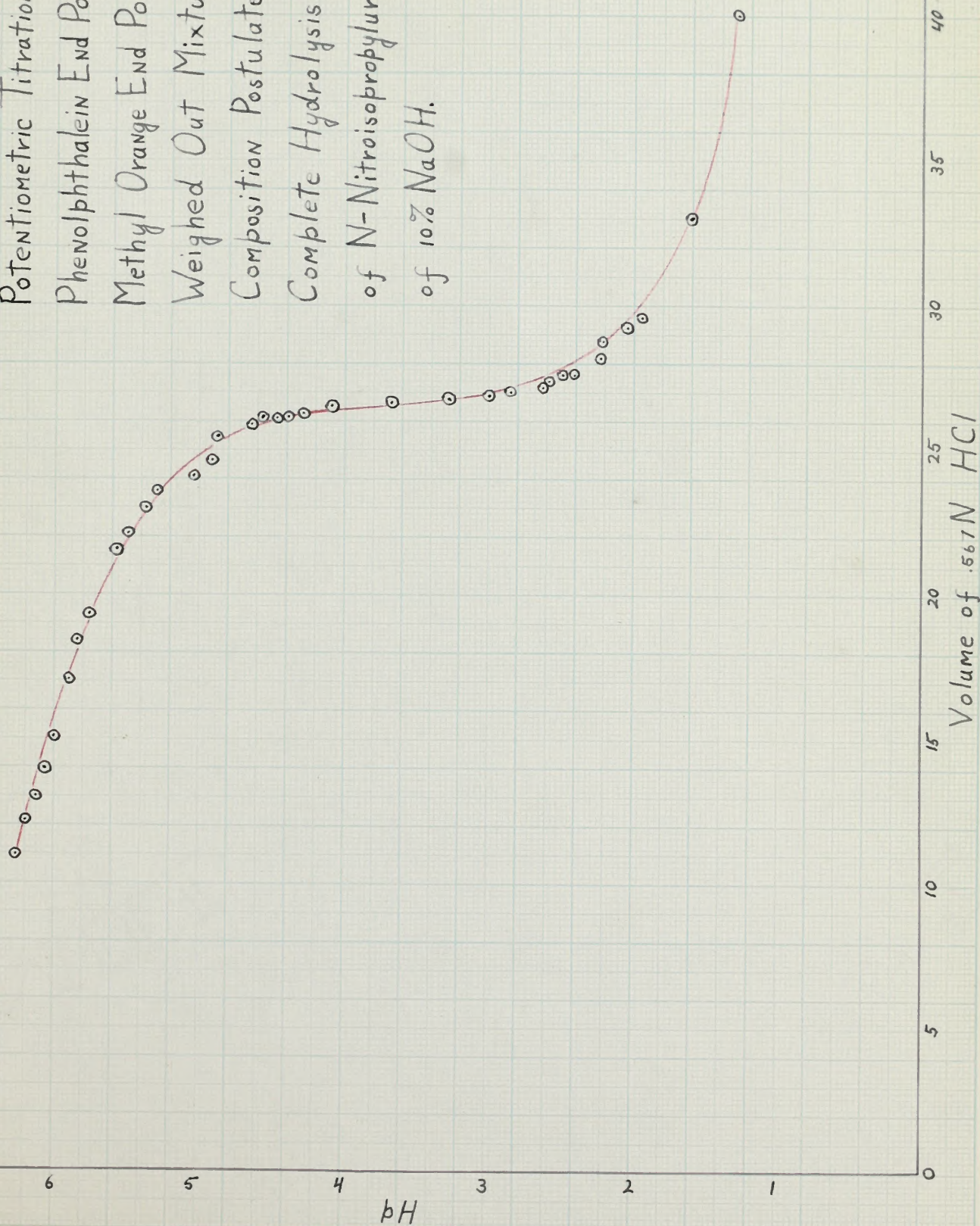
Weight of sample*   5.000 gr.

Theoretical CO_2: (5.000) (44/176) = 1.2500

(1.2500)/(44.00) = .00284 moles = 28.4 millimoles of CO_2

In a 50 c.c. aliquot there will be 28.4/4 = 7.10 millimoles

Total millimoles to be titrated (sodium salt of nitroamine

plus sodium carbonate) 2x7.10 = 14.20

From Figure I we observe that the volume of acid necessary to go from the

phenolphthalein end point to the methyl orange end point was 26.6 c.c.

The standard acid employed was .567 N.

(26.6) (.567) = 14.7 millimoles

Percentage Hydrolysis:

(100) (14.7) / (14.2) = 103%

Thus it seems evident that the composition of the reaction mixture after

hydrolysis is as postulated and that the analytical method employed is

correct within the limits of experimental error.

* Quantities of reagents based on this figure

Weight of sample* 5.000 gr.

Theoretical CO_2: (5.000) (44/176) = 1.2500

(1.2500)/(44.00) = .02284 moles = 28.4 millimoles of CO_2

In a 50 c.c. aliquot there will be 28.4/4 = 7.10 millimoles

Total millimoles to be titrated (sodium salt of nitrosamine

plus sodium carbonate) 2x7.10 = 14.20

From Figure I we observe that the volume of acid necessary to go from the

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IV. ACID HYDROLYSIS

A. Methods Employed:

In acid media the carbon dioxide produced by hydrolytic decomposition of the nitrourethan would of course be insoluble. Consequently it was planned to determine the percentage hydrolysis in acid solution by quantitative measurement of the carbon dioxide evolved from the reaction mixture. Sulfuric acid of varying concentrations was to be used as the hydrolysis medium. Three methods were employed for the collection of carbon dioxide; only one of which proved suitable for its quantitative determination under the conditions of the hydrolyses discussed below.

1. Adsorption on Ascarite.

Ascarite, asbestos particles impregnated with sodium hydroxide, is widely used in the determination of carbon in steel. This substance adsorbs quantitatively all of the carbon dioxide evolved when a small sample of steel is heated to a high temperature.

Accordingly it was thought that the carbon dioxide evolved in the nitrourethan hydrolysis could be collected in this manner.

The apparatus employed was set up as follows: A 500 c.c. three-necked flask, fitted with a gas inlet tube, a reflux condenser and a thermometer, was employed. The top of the condenser was connected to two calcium chloride tubes in series and from the second of the calcium chloride tubes a three foot length of rubber tubing led to a standard type Ascarite tube supported on a tripod.

To the gas inlet tube were connected in series an ascarite tube, a calcium chloride tube, a bubbling bottle and a nitrogen tank. The nitrogen was passed into the reaction vessel for the purpose of sweeping the

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To the gas inlet tube were connected in series an ascarite tube,
a calcium chloride tube, a bubbling bottle and a nitrogen tank. The nit-
rogen was passed into the reaction vessel for the purpose of sweeping the

carbon dioxide out of the flask and through the rest of the system. The calcium chloride tube was for the purpose of drying the nitrogen before it entered the Ascarite tube, for moisture might cause clogging to occur. The Ascarite tube was to remove any carbon dioxide from the nitrogen before it entered the reaction chamber.

One hundred cubic centimeters of sulfuric acid of the desired concentration was placed in the flask and a sample of the nitrourethan (about 10 grams) was weighed into the flask from a small dropping bottle.

The previously weighed Ascarite tube was attached to the end of the system and a slow stream of nitrogen was allowed to pass through. The flask was heated until the thermometer in the liquid registered 130° - $135^\circ C$. Heating was then continued for three hours. At the end of this time the carbon dioxide evolved was to be determined directly by the increase in weight of the Ascarite Tube.

Three runs only were made using this method and the following results were obtained: 10% H_2SO_4, 14.2% hydrolysis; 50% H_2SO_4, 98.6% and 115.5% hydrolysis. Examination of the Ascarite tube in the last two runs showed that small droplets of liquid were condensed on the sides of the tube in many places. Also at various points the Ascarite had taken on a dark brown tinge in contrast to its normal cream color. It was evident that some of the hydrolysis products or perhaps the nitrourethan itself was vaporizing and eluding the calcium chloride only to be trapped by the Ascarite. As a result the use of this method was discontinued.

2. <u>Absorption in Barium Hydroxide</u>:

It was thought that the extra weight of the Ascarite tube in the previous experiments might possibly be due to acidic oxides of nitrogen

carbon dioxide out of the flask and through the rest of the system. The

calcium chloride tube was for the purpose of drying the nitrogen before it-

entered the Ascarite tube, for moisture might cause clogging to occur. The

Ascarite tube was to remove any carbon dioxide from the nitrogen before it

entered the reaction chamber.

One hundred cubic centimeters of sulfuric acid of the desired con-

centration was placed in the flask and a sample of the nitrocellulose (about

10 grams) was weighed into the flask from a small dropping bottle.

The previously weighed Ascarite tube was attached to the end of

the system and a slow stream of nitrogen was allowed to pass through. The

Flask was heated until the thermometer in the liquid registered 130° - 135°C.

Heating was then continued for three hours. At the end of this time the

carbon dioxide evolved was to be determined directly by the increase in

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of the hydrolysis products or perhaps the nitrocellulose itself was vaporizing

and sinding the calcium chloride only to be trapped by the Ascarite. As a

result the use of this method was discontinued.

2. Absorption in Baryta Hydroxide:

It was thought that the extra weight of the Ascarite tube in the

previous experiments might possibly be due to acidic oxides of nitrogen

resulting from complete decomposition of the nitrourethan and its hydrolysis products by the sulfuric acid. Collection of the carbon dioxide evolved as barium carbonate seemed to offer a solution to this problem.

$$Ba(OH)_2 + CO_2 \longrightarrow \underline{BaCO_3} + H_2O$$

Any barium nitrate formed would be water soluble and not interfere in the gravimetric determination of the carbonate.

The apparatus was set up as for Ascarite adsorption with the exception that the two calcium chloride tubes between the reflux condenser and the receiving vessel were eliminated. The Ascarite tube was replaced by two 250 c.c. conical flasks containing 150 c.c. each of a saturated solution of barium hydroxide (15 grams in 300 c.c. of water). The reaction was carried out as before and after ten minutes a precipitate of barium carbonate began to appear in the absorption flasks. The gas issuing from the terminal flask was shown to be a mixture of nitrogen and carbon dioxide by allowing it to pass through a solution of barium hydroxide in a test tube, during which time a white precipitate of barium carbonate appeared.

The precipitate in the two flasks was collected on a Gooch crucible and dried at 110°C. Application of the appropriate calculations gave 23.7% hydrolysis for three hours refluxing with 50% sulfuric acid.

The low result is undoubtedly due to inefficient absorption of of the carbon dioxide. This could only be remedied by the employment of a large excess of the barium hydroxide solution which probably involves volumes of one or two liters, causing this method to become too unwieldy for quantitative work. This method was also abandoned in favor of that which follows.

3. <u>Absorption in Sodium Hydroxide:</u>

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Any barium nitrate formed would be water soluble and not interfere in the gravimetric determination of the carbonate.

The apparatus was set up as for Ascarite adsorption with the exception that the two calcium chloride tubes between the reflux condenser and the receiving vessel were eliminated. The Ascarite tube was replaced by two 250 c.c. conical flasks containing 150 c.c. each of a saturated solution of barium hydroxide (15 grams in 300 c.c. of water). The reaction was carried out as before and after ten minutes a precipitate of barium carbonate began to appear in the absorption flasks. The gas issuing from the terminal flask was shown to be a mixture of nitrogen and carbon dioxide by allowing it to pass through a solution of barium hydroxide in a test tube, during which time a white precipitate of barium carbonate appeared.

The precipitate in the two flasks was collected on a Gooch crucible and dried at 110°C. Application of the appropriate calculations gave 23.7% hydrolysis for three hours refluxing with 50% sulfuric acid.

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3. Absorption in Sodium Hydroxide:

Since it was shown in the previous experiment that collection in an alkaline solution is feasible, it was decided to try sodium hydroxide in place of the barium hydroxide. It was expected that the highly concentrated solutions of sodium hydroxide which it is possible to obtain would insure quantitative collection of the carbon dioxide. The carbon dioxide would, of course, be collected as sodium carbonate.

$$2NaOH + CO_2 \longrightarrow Na_2CO_3 + H_2O$$

Titration of the mixture to the phenolphthalein end-point would involve the following reactions.

$$NaOH + HCl \longrightarrow NaCl + H_2O$$

$$Na_2CO_3 + HCl \longrightarrow NaHCO_3 + NaCl$$

Continued titration with standard hydrochloric acid to the methyl orange end-point would bring about decomposition of the sodium bicarbonate.

$$NaHCO_3 + HCl \longrightarrow NaCl + H_2O + CO_2$$

Thus it was planned to titrate the carbon dioxide in a manner similar to the methods employed for basic hydrolysis.

The apparatus employed was identical with that used in the first two attempts with the exception that the absorption vessels in this case were four eight inch test-tubes containing 40 c.c. each of 35% sodium hydroxide solution.

The tubes which conducted the gas into the absorbing medium were drawn to fine capillaries in order to provide maximum surface for the reaction to take place.

At the end of the desired refluxing time, heating was discontinued and nitrogen was allowed to pass through the solution for the next fifteen minutes. The contents of the four test-tubes were then transferred quantitatively to a 500 c.c volumetric flask and diluted to volume with

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Continued titration with standard hydrochloric acid to the methyl orange

end-point would bring about decomposition of the sodium bicarbonate.

$$NaHCO_3 + HCl \longrightarrow NaCl + H_2O + CO_2$$

Thus it was planned to titrate the carbon dioxide in a manner similar to the

methods employed for basic hydrolysis.

The apparatus employed was identical with that used in the first

two attempts with the exception that the absorption vessels in this case

were four eight inch test-tubes containing 90 c.c. each of 33% sodium

hydroxide solution.

The tubes which conducted the gas into the absorbing medium were

drawn to fine capillaries in order to provide maximum surface for the

reaction to take place.

At the end of the desired refluxing time, heating was discon-

tinued and nitrogen was allowed to pass through the solution for the next

fifteen minutes. The contents of the four test-tubes were then transferred

quantitatively to a 500 c.c volumetric flask and diluted to volume with

distilled water. One-hundred cubic centimeter aliquot portions were then titrated to the phenolphthalein end-point with dilute hydrochloric acid and to the methyl orange end-point with standard hydrochloric acid(about .4N).

In all cases studied by this method a white precipitate invariably appeared in sodium carbonate, the solubility product of which had been exceeded in the strongly alkaline solution. It dissolved readily on di-lution.

4. Sample Calculation:

Data of the following type were employed for the calculation of the percentage hydrolysis in the runs described under "Absorption in Sodium Hydroxide" above.

Acid Hydrolysis of N-Nitroisopropylurethan

3 hours refluxing with 100 c.c. of 50% H_2SO_4

Wt. tube and sample	47.2652
Wt. tube	32.6412
Wt. sample	14.6240

$14.6240/4^*$ = 3.6560 grams of CO_2 available.

$3.6560/44$ = .08308 = 83.08 millimoles of CO_2

Since the total volume was 500 c.c., in a 100 c.c. aliquot there should be $83.08/5 = 16.61$ millimoles.

TITRATIONS

I		II	
End	39.52	End	39.46
Start	.09	Start	.35
	39.43		39.11

Average: 39.27

* See page 17

distilled water. One-hundred cubic centimeter aliquot portions were then

titrated to the phenolphthalein end-point with dilute hydrochloric acid and

to the methyl orange end-point with standard hydrochloric acid (about .4N).

In all cases studied by this method a white precipitate invariably

appeared in sodium carbonate, the solubility product of which had been

exceeded in the strongly alkaline solution. It dissolved readily on di-

lution.

4. Sample Calculation:

Data of the following type were employed for the calculation of

the percentage hydrolysis in the runs described under "Absorption in Sodium

Hydroxide" above.

Acid Hydrolysis of N-Nitrosomethylurethan

3 hours refluxing with 100 c.c. of 50% H_2SO_4

Wt. tube and sample	47.2552
Wt. tube	32.6212
Wt. sample	14.6340

14.6340/4 [*] = 3.6580 grams of CO_2 available.

3.6580/44 = .08308 = 83.08 millimoles of CO_2

Since the total volume was 500 c.c., in a 100 c.c. aliquot there should be

83.08/5 = 16.61 millimoles.

TITRATIONS

	I		II
End	39.52	End	39.46
Start	.09	Start	.35
	39.43		39.11

Average: 39.27

The standard hydrochloric used was .4012N

$$(39.27)(.4012) = 15.8 \text{ millimoles}$$

Thus:

Percentage Hydrolysis $(100)(15.8)/(16.6) = 95.2\%$

The results obtained by application of the above calculations are tabulated

below. The reactions were carried out at about $130^{\circ}-135^{\circ}C$.

TABLE V

PERCENTAGE HYSROLYSIS IN ACID MEDIUM

% H_2SO_4	TIME	% HYDROLYSIS
50%	3 hrs.	95.2%
50%	1 hr.	79.8%
50%	½ hr.	74.4%
20%	6 hrs.	73.5%
10%	8 hrs.	28.7%
5%	8 hrs.	21.5%
5%	8 hrs.	26.0%
50% CH_3COOH	4 hrs.	26.3%

B. Tetranitromethane:

When the acid used for hydrolysis was 20% H_2SO_4 or over, the

liquid in the absorption tubes took on an intense yellow color. It was

postulated that this might be due to the presence of tetranitromethane in

the nitrourethan. This compound might be formed in small quantities by

reaction of the acetic anhydride with the fuming nitric acid during nitration

of the isopropylurethan.

$$(CH_3CO)_2O + 8HONO_2 \longrightarrow 2C(NO_2)_4 + 2CO_2 + 7HOH$$

Hydrolysis of this tetranitromethane would then occur simultaneously with

The standard hydrochloric used was .4012N

(35.27)(.4012) = 15.8 millimoles

Thus:

Percentage Hydrolysis (100)(15.8)/(16.6) = 95.2%

The results obtained by application of the above calculations are tabulated below. The reactions were carried out at about 150°-135°C.

TABLE V

PERCENTAGE HYDROLYSIS IN ACID MEDIUM

% H_2SO_4	TIME	% HYDROLYSIS
50%	3 hrs.	95.2%
50%	1 hr.	79.6%
50%	½ hr.	74.4%
20%	6 hrs.	73.5%
10%	8 hrs.	28.7%
5%	8 hrs.	21.3%
2%	8 hrs.	26.0%
50% CH_3COOH	4 hrs.	26.3%

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liquid in the absorption tubes back on an intense yellow color. It was

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reaction of the acetic anhydride with the fuming nitric acid during nitration

of the isopropylurethan.

$$(CH_3CO)_2O + 4HNO_3 \longrightarrow 2C(NO_2)_4 + 2SO_2 + HCOH$$

Hydrolysis of this tetranitromethane would then occur simultaneously with

that of the nitrourethan to yield nitroform.

$$C(NO_2)_4 + HOH \longrightarrow H-C(NO_2)_3 + HONO_2$$

This nitroform might conceivably pass through the condenser in small quantities and react with the sodium hydroxide to form its sodium salt which is highly colored.

$$H-C(NO_2)_3 + NaOH \longrightarrow NaC(NO_2)_3 + HOH$$

However, a brown ring test on the residue of several of the runs described wwas negative. On this basis it was concluded that if tetranitromethane were present, its amount was negligible.

In order to test the foregoing hypothesis, tetranitromethane was prepared by the method of Chatterway (2).

To 31 grams of nitric acid (sp.gr.1.53) was added gradually 50 grams of acetic anhydride. The flask was cooled so that the temperature did not go above $20^{\circ}-25^{\circ}C$. The flask was stoppered loosely and allowed to stand at room temperature for about a week. As the reaction proceeded, carbon dioxide was slowly evolved and the colorless mixture became brown due to the presence of oxides of nitrogen. After one week the mixture was poured into 200 c.c. of water. Tetranitromethane separated. The oil was washed with water until it was free from acid.

Chatterway (2.) mentions that tetranitromethane can also be freed from acids by steam distillation although some nitroform is formed in this operation and imparts a bright yellow color. Thus it seems evident that nitroform would assuredly be formed under the conditions employed in the present work.

Four drops (.2c.c.) of the tetranitromethane were refluxed for two hours in the apparatus used for hydrolysis of the nitrourethan. No precipitate appeared in the absorption tubes during this time (See page 26)

that of the nitromethane to yield nitroform.

$$C(NO_2)_4 + HOH \longrightarrow H-C(NO_2)_3 + HONO_2$$

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did not go above 20°-25°C. The flask was stoppered loosely and allowed to
stand at room temperature for about a week. As the reaction proceeded,
carbon dioxide was slowly evolved and the colorless mixture became brown
due to the presence of oxides of nitrogen. After one week the mixture was
poured into 300 c.c. of water. Tetranitromethane separated. The oil was
washed with water until it was free from acid.

Chattaway (2.) mentions that tetranitromethane can also be freed
from acids by steam distillation although some nitroform is formed in this
operation and imparts a bright yellow color. Thus it seems evident that
nitroform would assuredly be formed under the conditions employed in the
present work.

Four drops (2c.c.) of the tetranitromethane were refluxed for
two hours in the apparatus used for hydrolysis of the nitromethan. No
precipitate appeared in the absorption tubes during this time (See page 24.)

but the solution took on an intense yellow color exactly like that observed
when the nitrourethan was hydrolyzed. This time a brown ring test on the
hydrolysis medium was positive. Thus we may conclude that the amount of
tetranitromethane in the sample of isopropylnitrourethan used is considerably
less than .2 c.c.

C. Further Hydrolysis:

It was thought that the nitroamine formed by hydrolysis of the
nitrourethan might undergo further hydrolysis to yield the amine and nitric
acid.

$$(CH_3)_2 \overset{H}{C}NH-NO_2 \, \slash \, HOH \longrightarrow (CH_3)_2 \overset{H}{C}NH_2 \, \slash \, HONO_2$$

Although this reaction was shown not to occur to any appreciable extent in
basic solution, it seemed desirable to determine whether or not it did take
place in acid solution.

Attempts to get a brown-ring test on the acid residues from the
various hydrolyses failed, so we may conclude that this reaction does not
take place under the conditions herein described.

D. Inhibition:

As mentioned in the introduction, (page 8) it was planned to add
certain reagents capable of utilizing the unshared pair on the amino nitrogen
in the nitrourethan molecule. It was decided to employ acid of the lowest
concentration possible so that there would be less danger of any weak bond
being disrupted by the hot acid. The results tabulated on page 28 indicated
that probably eight hours refluxing with 5% H_2SO_4 would be suitable condit-
ions for this investigation.

It was found that gentle refluxing could be induced in acid of
this low concentration at about 110°C. Accordingly the flask was heated
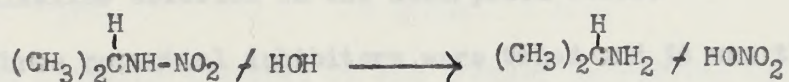with an oil-bath maintained at 115°C. The thermometer inside the flask was

but the solution took on an intense yellow color exactly like that observed

when the nitrourethan was hydrolyzed. This time a brown ring test on the

hydrolysis medium was positive. Thus we may conclude that the amount of

tetranitromethane in the sample of isopropylnitrourethan used is considerably

less than 2 c.c.

C. Further Hydrolysis:

It was thought that the nitrosamine formed by hydrolysis of the

nitrourethan might undergo further hydrolysis to yield the amine and nitric

acid.

$$(CH_3)_2\overset{H}{C}NH-NO_2 + HOH \longrightarrow (CH_3)_2\overset{H}{C}NH_2 + HONO_2$$

Although this reaction was shown not to occur to any appreciable extent in

basic solution, it seemed desirable to determine whether or not it did take

place in acid solution.

Attempts to get a brown-ring test on the acid residues from the

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certain reagents capable of utilizing the unshared pair on the amino nitrogen

in the nitrourethan molecule. It was decided to employ acid of the lowest

concentration possible so that there would be less danger of any weak bond

being disrupted by the hot acid. The results tabulated on page 27 indicated

that probably eight hours refluxing with 5% H_2SO_4 would be suitable condit-

ions for this investigation.

It was found that gentle refluxing could be induced in acid of

this low concentration at about 110°. Accordingly the flask was heated

with an oil-bath maintained at 115°C. The thermometer inside the flask was

omitted.

It was decided to employ stirring, for in some of the test runs it was found that contact between the nitrourethan and the inhibitor could not be effected in the absence of agitation. For example, the nitrourethan floated on the surface of the acid but an inhibitor such as chloroform sank to the bottom so that contact was prevented.

Accordingly a mercury-sealed stirrer was employed. Enough mercury was used in the trap to withstand the pressure of approximately sixteen inches of alkaline solution in the absorption tubes.

Three potential inhibitors were tried and it was thought that they might utilize the unshared electron-pair on the amino nitrogen and thus prevent attachment of the proton (the postulated initial step in the hydrolysis) from occurring.) The equations below illustrate this.

1. Chloroform:

$$(CH_3)_2CH-\overset{NO_2}{\underset{H}{N}}-\overset{O}{\overset{\shortparallel}{C}}-O-C_2H_5 + H-C-Cl_3 \longrightarrow (CH_3)_2CH-\overset{NO_2}{\underset{H-CCl_3}{N}}--\overset{O}{\overset{\shortparallel}{C}}--O-C_2H_5$$

2. Cholesterol:

$$(CH_3)_2-CH-\overset{NO_2}{\underset{}{N}}--COOC_2H_5 + R : \overset{..}{\underset{}{O}} : H \longrightarrow (CH_3)_2-CH-\overset{NO_2}{\underset{H : O : R}{N}}--COOC_2H_5$$

R = Parent hydrocarbon structure of cholesterol.

3. Boric Acid:

$$(CH_3)_2CH-\overset{NO_2}{\underset{}{N}}--\overset{O}{\overset{\shortparallel}{C}}--O-C_2H_5 + \overset{H}{\underset{\underset{H}{\overset{O}{|}}}{B}}-O \quad H \longrightarrow (CH_3)_2-CH-\overset{NO_2}{\underset{H \ O-B-O \ H}{N}}--\overset{O}{\overset{\shortparallel}{C}}--OC_2H_5$$

The results obtained on the basis of these postulated mechanisms are tabulated below:
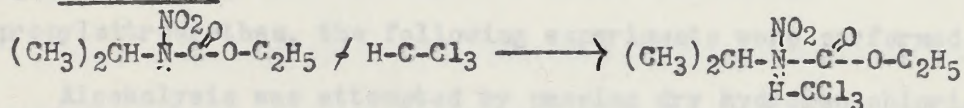
omitted.

It was decided to employ slow stirring, for in some of the last runs

it was found that contact between the nitromethane and the inhibitor could

not be affected in the absence of agitation. For example, the nitromethane

floated on the surface of the acid but an inhibitor such as chloroform

sank to the bottom so that contact was prevented.

Accordingly a mercury-sealed stirrer was employed. Enough mercury

was used in the trap to withstand the pressure of approximately sixteen

inches of alkaline solution in the absorption tubes.

Three potential inhibitors were tried and it was thought that they

might utilize the unshared electron-pair on the amino nitrogen and thus

prevent attachment of the proton (the postulated initial step in the

hydrolysis) from occurring. The equations below illustrate this.

1. Chloroform:

$$(CH_3)_2CH-N \overset{NO_2}{\underset{}{-C-O-CH_2C_6H_5}} + H-C-Cl_3 \longrightarrow (CH_3)_2CH-N-C-O-CH_2C_6H_5$$

2. Cholesterol:

$$(CH_3)_2CH-N-C-O-CH_2C_6H_5 + R \cdot OH \longrightarrow (CH_3)_2CH-N-C-OOC_6H_5$$

R = Parent hydrocarbon structure of cholesterol.

3. Boric Acid:

$$(CH_3)_2CH-N-C-O-CH_2C_6H_5 + H-O-B-O-H \longrightarrow (CH_3)_2CH-N-C-O-CH_2C_6H_5$$

The results obtained on the basis of these postulated mechanisms

are tabulated below:

TABLE VI

PERCENTAGE HYDROLYSIS WITH ATTEMPTED INHIBITION

% H_2SO_4	INHIBITOR	AMOUNT	TIME	% HYDROLYSIS
5%	None		7 hrs.	14.9%
5%	None		7 hrs.	15.8%
5%	$CHCl_3$	7 c.c.(1md.eg.)	7 hrs.	16.7%
5%	Cholesterol	1.5 grams	7 hrs.	15.9%
5%	Cholesterol	1.5 grams	7 hrs.	15.9%
5%	H_3BO_3	5 grams	7 hrs.	15.6%

Obviously the reagents employed do not prevent hydrolysis to any degree
which is detectable by the methods used.

E. ACID ALCOHOLYSIS:

In an attempt to determine the true mechanism of the acid hydrolysis
of isopropylnitrourethan, the following experiments were performed.

Alcoholysis was attempted by passing dry hydrogen chloride gas
through an alcoholic solution of the nitrourethan. It was postulated that
if alcoholysis proceeded by the mechanism whereby the proton attacks the
amino nitrogen atom (page 6), that the products of the reaction would be
diethyl carbonate and isopropyl nitroamine.
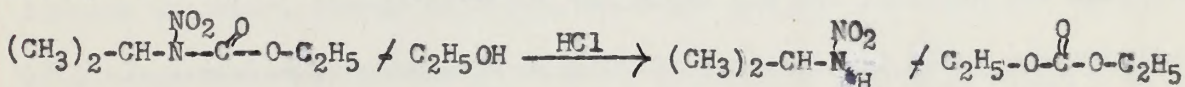
$$(CH_3)_2-CH-N(NO_2)-C(O)-O-C_2H_5 \neq C_2H_5OH \xrightarrow{HCl} (CH_3)_2-CH-N(NO_2)(H) \neq C_2H_5-O-C(O)-O-C_2H_5$$

On the other hand if the reaction proceeded by the accepted
mechanism of ester hydrolysis (page 7) the overall result would be no
different products.

In preparation for this investigation, diethyl carbonate was
distilled under reduced pressure and was found to have a boiling point
of 57°C @ 50mm.

TABLE VI

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Alcoholysis was attempted by passing dry hydrogen chloride gas through an alcoholic solution of the nitrourethan. It was postulated that if alcoholysis proceeded by the mechanism whereby the proton attacks the amino nitrogen atom (page 5), that the products of the reaction would be diethyl carbonate and isopropyl nitrosamine.

$$(CH_3)_2\text{-CH-N-}\overset{O}{C}\text{-O-}C_2H_5 + C_2H_5OH \underset{H^+}{\overset{NO_2}{\rightleftharpoons}} (CH_3)_2\text{-CH-N-} \xleftarrow{HCl} C_2H_5\text{-O-}\overset{O}{C}\text{-O-}C_2H_5$$

On the other hand if the reaction proceeded by the accepted mechanism of ester hydrolysis (page 7) the overall result would be no different products.

In preparation for this investigation, diethyl carbonate was distilled under reduced pressure and was found to have a boiling point of 37°C @ 50mm.

The reaction was carried out as follows:

Twenty grams of isopropylnitrourethan was placed in a 200 c.c. round bottom-
ed flask and 50 c.c. of absolute ethanol was added. A current of dry HCl
was passed through this mixture for a period of two hours. At first a good
deal of heat was evolved and gentle refluxing was evident in the solution.
After about thirty minutes the exothermic reaction subsided and at the end
of the two hour period the flask and its contents were at room temperature.

The mixture was transferred to a Claisen flask and distilled under
reduced pressure. The first fraction, ethyl alcohol passed over at 33°C @
50 mm. Then there was a sharp rise to approximately 85°C. Since there was
no fraction boiling at 57°C (diethyl carbonate) and none boiling over 90°C
(isopropylnitroamine) we may conclude that these substances were not present.

Thus it would seem that the mechanism of nitrourethan hydrolysis
is closely similar to that accepted for ester hydrolysis.

When a current of dry HCl was passed through absolute ethanol a
good deal of heat was evolved, indicating that the heat observed was merely
the heat of solution of HCl in ethanol.

The reaction was carried out as follows:

Twenty grams of isopropylnitrourethan was placed in a 200 c.c. round bottom flask and 50 c.c. of absolute ethanol was added. A current of dry HCl was passed through this mixture for a period of two hours. At first a good deal of heat was evolved and gentle refluxing was evident in the solution. After about thirty minutes the exothermic reaction subsided and at the end of the two hour period the flask and its contents were at room temperature. The mixture was transferred to a Claisen flask and distilled under reduced pressure. The first fraction, ethyl alcohol passed over at 33°C @ 50 mm. Then there was a sharp rise to approximately 83°C. Since there was no fraction boiling at 57°C (diethyl carbonate) and none boiling over 90°C (isopropylnitrourethan) we may conclude that these substances were not present. Thus it would seem that the mechanism of nitrourethan hydrolysis is closely similar to that accepted for ester hydrolysis.

When a current of dry HCl was passed through absolute ethanol a good deal of heat was evolved, indicating that the heat observed was merely the heat of solution of HCl in ethanol.

V ISOPROPYLNITROAMINE:

A. Isolation:

As was predicted in the introduction to this Thesis (page 6),
isopropylnitroamine was found to be one of the products of the hydrolysis of
isopropylnitrourethan. It was extracted from both acidic and basic hydroly-
sis mixtures by shaking with ether. The basic mixtures were acidified
before ether extraction. When distilled under reduced pressure the compound
passed over at the temperature recorded by Thomas (12.), 90° @ 10mm.

B. Preparation:

The procedure which was employed for the hydrolysis of large
quantities of N-Nitroisopropyl urethan is as follows.

One equivalent of isopropylnitrourethan (176gr.) was placed in a
one liter round-bottomed flask containing 4 equivalents of sodium hydroxide
in the form of a 35% solution. (160 grams of NaOH in 290 c.c. of water).
Three equivalents of sodium hydroxide are necessary for complete hydrolysis
(page 16), the fourth equivalent was added to insure rapidity of hydrolysis.

The flask was then connected to a reflux condenser and was heated
for four hours, At the end of this time the heating was discontinued and
the mixture allowed to cool to room temperature. Two or three cubic cent-
imeters of methyl orange solution was added and the solution was acidified
with concentrated hydrochloric acid until a bright red color was obtained.

The acidic mixture was then allowed to cool to room temperature.
It was transferred to a two-liter separatory funnel and extracted with
3-300 c.c. portions of ether. The ether layer was dried with 50 grams of
anhydrous sodium sulfate and the ether was distilled on a steam bath. The
residue was a light brown oil.

The oil was distilled under reduced pressure and passed over at

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B. Preparation:

The procedure which was employed for the hydrolysis of large quantities of N-Nitroisopropyl urethan is as follows.

One equivalent of isopropylnitrourethan (1Vógr.) was placed in a one liter round-bottomed flask containing 4 equivalents of sodium hydroxide in the form of a 35% solution. (180 grams of NaOH in 390 c.c. of water).
Three equivalents of sodium hydroxide are necessary for complete hydrolysis (page 6), the fourth equivalent was added to insure rapidity of hydrolysis.
The flask was then connected to a reflux condenser and was heated for four hours. At the end of this time the heating was discontinued and the mixture allowed to cool to room temperature. Two or three cubic centi-meters of methyl orange solution was added and the solution was acidified with concentrated hydrochloric acid until a bright red color was obtained.
The acidic mixture was then allowed to cool to room temperature.

It was transferred to a two-liter separatory funnel and extracted with 3-300 c.c. portions of ether. The ether layer was dried with 50 grams of anhydrous sodium sulfate and the ether was distilled on a steam bath. The residue was a light brown oil.

The oil was distilled under reduced pressure and passed over at

89°C under a pressure of 8mm. The product, isopropylnitroamine, was a water-white liquid with a faintly sweet odor.

The molecular weight of isopropylnitroamine is 104. The yield was 79 grams (76%).

When 288 grams of isopropylnitrourethan was hydrolyzed by this method in a five liter flask a yield of nitroamine corresponding to only 40% of the theoretical was obtained. Evidently the condenser was not efficient enough to take care of the large boiling surface.

Isopropylnitroamine has been extracted from some of the acidic hydrolysis mixtures and has been identified by its boiling point and odor. The same method that was used for extraction of the nitroamine from basic media was employed. Of course acidification is unnecessary.

C. Preparation of Derivatives:

Aside from metallic salts prepared by Thomas (12.) and others (page 4) no solid derivatives suitable for identification of nitroamines have been recorded in the literature. Thus it seemed desirable to attempt to prepare a series of compounds with this purpose in mind.

Although the nitroamine is an acidic substance it was thought that it might react with the acid chlorides which are ordinarily employed for the preparation of solid derivatives of primary and secondary amines. Accordingly attempts were made to bring about a reaction between the nitroamine and such acidic reagents as benzenesulfonyl chloride, p-bromobenzene-sulfonyl chloride and benzoyl chloride. Failing to effect a reaction with any of these reagents, basic reagents were turned to. Two of these reagents, morpholine and piperazine yielded satisfactory solid salts. The results of this investigation are discussed more completely below.

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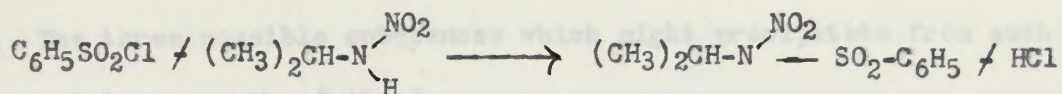to prepare a series of compounds with this purpose in mind.

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sulfonyl chloride and benzoyl chloride. Failing to effect a reaction with

any of these reagents, basic reagents were turned to. Two of these reagents,

morpholine and piperidine yielded satisfactory solid salts. The results of

this investigation are discussed more completely below.

1. Benzenesulfonyl chloride (10.)

Equivalent amounts of benzenesulfonyl chloride and isopropylnitro-
amine were mixed with 50 c.c. of 10% sodium hydroxide solution. On shaking,
much heat was evolved. It was thought that the following reaction might
have occurred.

$$C_6H_5SO_2Cl \;/\; (CH_3)_2CH-N\overset{NO_2}{\underset{H}{\diagdown}} \longrightarrow (CH_3)_2CH-N\overset{NO_2}{\diagup} - SO_2-C_6H_5 \;/\; HCl$$

However, precipitation did not occur on cooling the reaction mixture in an
ice salt bath and no precipitate appeared when a small portion of the mixture
was acidified in a test-tube.

The reaction mixture was then extracted with three 20 c.c. portions
of ether. The ether extract was set aside to evaporate. No residue re-
mained in the evaporating dish after evaporation of the ether. The heat
evolved must have been merely a result of the hydrolysis of the acid chloride.
Similar observations were made on a blank run. The N-Nitrobenzene sulfon-
amide of isopropyl nitroamine has been prepared by Zsolonina (17.) by
reacting the isopropyl amine with benzenesulfonyl chloride and nitrating
the resulting product. The compound had a melting point of 34°-35°C.

2. Benzoyl chloride: (10.)

The same procedure that was used with benzenesulfonyl chloride was
followed with benzoyl chloride. Evaporation of the ether extract again
yielded no residue.

3. p-Bromobenzenesulfonyl chloride: (10.)

Two grams of isopropylnitroamine and five grams of p-bromobenzene
sulfonyl chloride were added to 30 c.c of 10% NaOH. No reaction occurred in
the cold, the solid acid chloride merely settling to the bottom of the flask.
On heating the acid chloride melted and slowly went into solution (about 15 min.).

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$$C_6H_5SO_2Cl + (CH_3)_2CH-N\overset{NO_2}{} \longrightarrow (CH_3)_2CH-N\overset{NO_2}{\underset{H}{}}-SO_2-C_6H_5 + HCl$$

However, precipitation did not occur on cooling the reaction mixture in an
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the cold, the solid acid chloride merely settling to the bottom of the flask.
On heating the acid chloride melted and slowly went into solution (about 15 min.).

When the acid chloride had dissolved completely, the solution was still alkaline.

On cooling of the reaction mixture white crystals separated. These crystals were soluble in water, insoluble in ether and would not burn; suggesting a salt rather than a sulfonamide. The crystals were filtered and dried. The three possible substances which might precipitate from such a reaction mixture are the following:

$$Br-C_6H_5-SO_2-ONa, \quad Br-C_6H_5-SO_2-N(NO_2)(CH_3)_2, \quad (CH_3)_2CH-N(NO_2)Na$$
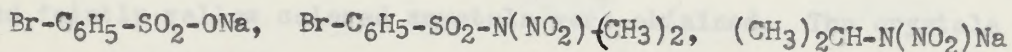
It is obvious that qualitative analysis for the elements nitrogen, sulfur and bromine would serve to distinguish the product. Accordingly sodium fusion was performed and these elements were tested for using the methods described by Shriner and Fuson (10.).

The qualitative tests indicated the presence of sulfur and bromine only. The crystals were therefore the sodium salt of p-bromobenzenesulfonic acid, $Br-C_6H_5-SO_2-ONa$, and it is clear that the only reaction which occurred was hydrolysis of the acid chloride.

Similar observations were made on a blank run. The blank run was carried out as just described above with the exception that the isopropylnitroamine was withheld

4. Morpholine:

After failing in attempts to bring about reactions with various acidic reagents which usually react with amines it was decided to try basic reagents in the hope that they would yield salts with the acidic nitroamine.

The first of the basic reagents employed was morpholine. It was decided to mix ethereal solutions of the two reactants and if a salt like

derivative formed, it was thought that it would precipitate. Accordingly
equal volumes (1 c.c.) of morpholine and isopropylnitroamine were dissolved
separately in 3 c.c. portions of ether. The two solutions were mixed and a
rather vigorous exothermic reaction took place causing the ether to boil.
The mixture became rather viscous but precipitation did not occur. It is
noteworthy that the proportion of reactants employed corresponds to a con-
siderable excess of the nitroamine. The mixture was set aside to evaporate
and faintly yellow colored crystals were obtained. The crystals were washed
with ether by suction. M.P. 65-68°C.

The following procedure was employed for preparing this compound
in larger quantity and greater degree of purity. Since an excess of nitro-
amine seemed to retard precipitation, it was decided to employ an excess of
morpholine, the latter being more readily volatile than the nitroamine. The
molecular weight of isopropylnitroamine is 104, that of morpholine 87.

$$104/87 = 1.21 \text{ gr. nitroamine/gr.morpholine}$$

In order to insure an excess of morpholine five grams of this compound were
added to 50 c.c. of ether and five grams of isopropylnitroamine were added
dropwise. The reaction was observed to be exothermic but in this case not
violent enough to bring about ebullition of the solvent. Precipitation did
not occur immediately. The mixture was set aside and after about ten min-
utes precipitation began to take place in such a rapid manner that little
waves were created on the surface of the liquid. The crystals were filtered
off by suction and washed with two 20 c.c. portions of ether. The yield
was nine grams (about 100%).

Properties: Soluble in water, insoluble in ether. Crystals are scaly
    in appearance. Water solutions of this compound are neutral to litmus,
    methyl orange and phenolphthalein. M.P. 69°-70°C.

It is thought that the equation for the reaction may be written as follows.

$$\begin{matrix} CH_3 \\ CH-N \\ CH_3 \end{matrix}\begin{matrix} NO_2 \\ \\ H \end{matrix} + H-N\begin{matrix} CH_2-CH_2 \\ \\ CH_2-CH_2 \end{matrix}O \longrightarrow \left[\begin{matrix} CH_3 \\ CH-N: \\ CH_3 \end{matrix}NO_2\right]\left[\begin{matrix} H \\ N \\ H \end{matrix}\begin{matrix} CH_2-CH_2 \\ \\ CH_2-CH_2 \end{matrix}O\right]^{+}$$

Actually an acid-base reaction has taken place and the result is a salt.
The compound has a molecular weight, as calculated from the formula, of 191.
Results of analysis for carbon and hydrogen are shown below.

	Carbon	Hydrogen
Calculated	44.0%	8.9%
Observed	43.77%	9.12%
Observed	43.81%	9.30%

5. Piperazine:

A similar reaction was effected with piperazine. The reaction,
however, had to be carried out in alcohol because the piperazine is insoluble
in ether. There are two possible reaction products in this case since the
piperazine ring contains two secondary amino groups. The reaction can
theoretically proceed by either of the following two paths.

(1.) $$\begin{matrix} CH_3 \\ CH-N \\ CH_3 \end{matrix}\begin{matrix} NO_2 \\ \\ H \end{matrix} + H-N\begin{matrix} CH_2-CH_2 \\ \\ CH_2-CH_2 \end{matrix}N-H \longrightarrow \left[\begin{matrix} CH_3 \\ CH-N: \\ CH_3 \end{matrix}NO_2\right]^{-}\left[\begin{matrix} H \\ N \\ H \end{matrix}\begin{matrix} CH_2-CH_2 \\ \\ CH_2-CH_2 \end{matrix}N-H\right]^{+}$$
I

(2) $$2\begin{matrix} CH_3 \\ CH-N \\ CH_3 \end{matrix}\begin{matrix} NO_2 \\ \\ H \end{matrix} + H-N\begin{matrix} CH_2-CH_2 \\ \\ CH_2-CH_2 \end{matrix}N-H \longrightarrow \left[\begin{matrix} CH_3 \\ CH-N: \\ CH_3 \end{matrix}NO_2\right]^{-}\left[\begin{matrix} H \\ N \\ H \end{matrix}\begin{matrix} CH_2-CH_2 \\ \\ CH_2-CH_2 \end{matrix}\begin{matrix} H \\ N \\ H \end{matrix}\right]^{++}\left[\begin{matrix} NO_2 \\ :N-CH \end{matrix}\begin{matrix} CH_3 \\ \\ CH_3 \end{matrix}\right]^{-}$$
II

The fact that the reaction product was neutral in its water solutions to
litmus is good evidence for compound II because compound I which has one
free amino group as does morpholine whould be basic to litmus as is morpholine.

The method of preparing the compound was as follows: Three grams
of piperazine were dissolved in 40 c.c. of ethyl alcohol since piperazine is

It is thought that the equation for the reaction may be written as follows.

$$\text{CH}_3-\text{CH} \Big\langle {}^{\text{NO}_2}_{\text{CH}_3} + \text{H-N} \Big\langle {}^{\text{CH}_2-\text{CH}_2}_{\text{CH}_2-\text{CH}_2} \rangle \text{O} \longrightarrow \left[\begin{array}{c} \text{CH}_3 \\ \text{CH-N:} \\ \text{CH}_3 \end{array} \right]^{-} \left[\text{H-N} \Big\langle {}^{\text{CH}_2-\text{CH}_2}_{\text{CH}_2-\text{CH}_2} \rangle \text{O} \right]^{+}$$

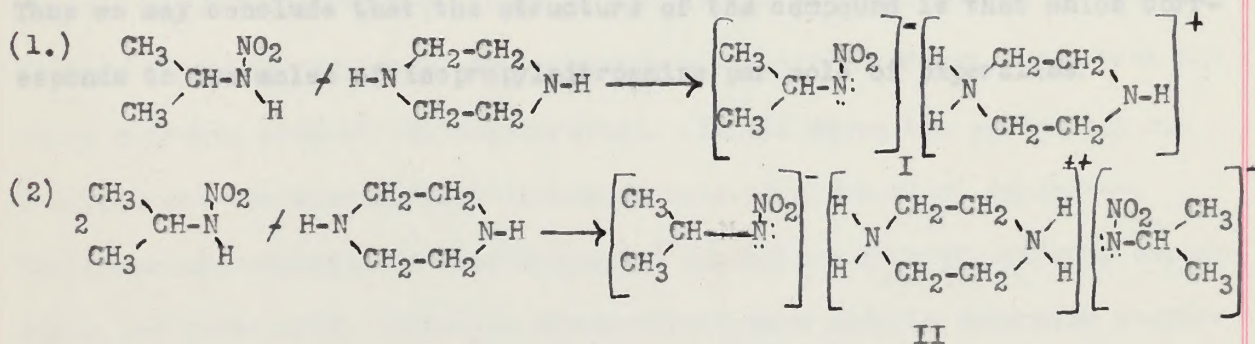Actually an acid-base reaction has taken place and the result is a salt.

The compound has a molecular weight, as calculated from the formula, of 191.

Results of analysis for carbon and hydrogen are shown below.

	Carbon	Hydrogen
Calculated	44.0%	8.9%
Observed	43.77%	9.12%
Observed	43.81%	9.30%

5. Piperazine:

A similar reaction was effected with piperazine. The reaction, however, had to be carried out in alcohol because the piperazine is insoluble in ether. There are two possible reaction products in this case since the piperazine ring contains two secondary amino groups. The reaction can theoretically proceed by either of the following two paths.

(1.) $\text{CH}_3-\text{CH} \Big\langle {}^{\text{NO}_2}_{\text{CH}_3} + \text{H-N} \Big\langle {}^{\text{CH}_2-\text{CH}_2}_{\text{CH}_2-\text{CH}_2} \rangle \text{N-H} \longrightarrow$ I

(2) $2 \, \text{CH}_3-\text{CH} \Big\langle {}^{\text{NO}_2}_{\text{CH}_3} + \text{H-N} \Big\langle {}^{\text{CH}_2-\text{CH}_2}_{\text{CH}_2-\text{CH}_2} \rangle \text{N-H} \longrightarrow$ II

The fact that the reaction product was neutral in litmus solutions to litmus is good evidence for compound II because compound I which has one free amino group as does morpholine would be basic to litmus as is morpholine.

The method of preparing the compound was as follows: Three grams of piperazine were dissolved in 40 c.c. of ethyl alcohol since piperazine is

insoluble in ether. Vigorous stirring was necessary to effect complete sol-
ution. Nine grams of isopropylnitroamine (enough to react with both amino
groups) was added to the solution. The mixture was then poured into 500 c.c.
of ether and voluminous precipitation occurred. The mixture was filtered
by suction and the feathery crystals were washed with two 20 c.c. portions
of ether. The yield was about four grams (57% or 36% depending upon struct-
ure). An additional two grams of product was obtained on evaporation of the
ether-alcohol mixture. (Total yield 65%). This last compound melted around
113°C whereas the precipitated compound melted at about 114°C. The molecular
weights postulated are I, 190; II, 294.

Results of carbon-hydrogen analysis are as follows:

	Carbon	Hydrogen
Calculated I	44.0%	9%
Calculated II	40.8%	8.85%
Observed	40.89%	9.22%
Observed	40.99%	9.06%

Thus we may conclude that the structure of the compound is that which corr-
esponds to two moles of isopropylnitroamine per mole of piperazine.

insoluble in ether. Vigorous stirring was necessary to effect complete sol-
ution. Nine grams of isopropylnitrosamine (enough to react with both amino
groups) was added to the solution. The mixture was then poured into 500 c.c.
of ether and voluminous precipitation occurred. The mixture was filtered
by suction and the leathery crystals were washed with two 20 c.c. portions
of ether. The yield was about four grams (57% or 36% depending upon struct-
ure). An additional two grams of product was obtained on evaporation of the
ether-alcohol mixture. (Total yield 65%). This last compound melted around
115°C whereas the precipitated compound melted at about 116°C. The molecular
weights postulated are I, 190; II, 294.

Results of carbon-hydrogen analysis are as follows:

	Carbon	Hydrogen
Calculated I	44.0%	9%
Calculated II	40.8%	8.83%
Observed	40.83%	9.22%
Observed	40.99%	9.08%

Thus we may conclude that the structure of the compound is that which corr-
esponds to two moles of isopropylnitrosamine per mole of piperazine.

VI SUMMARY

The information recorded in the previous pages may be summarized as follows.

N-Nitroisopropylurethan has been subjected to hydrolysis in both basic and acidic media, varying the concentration of the hydrolyzing agent as well as the time of contact with this reagent.

As a general rule the nitrourethan is more easily hydrolyzed by acids than by bases, i.e. in a given time interval a given concentration of sodium hydroxide will give a greater degree of hydrolysis than the same concentration of sulfuric acid.

The mechanism of this hydrolytic splitting has been discussed in detail and it was concluded that probably the attack of the acidic and basic reagents takes place at the carbonyl group as in ordinary ester hydrolysis rather than at the amino nitrogen atom as was first postulated for acid hydrolysis.

In order to test the postulated mechanism of acid hydrolysis, certain reagents were to be added to the hydrolysis mixtures in an attempt to form addition compounds, or compounds containing hydrogen bonds with the amino nitrogen atom of the nitrourethan. In all cases the percentage hydrolysis was the same as that in the absence of a potential inhibitor. The compounds employed in this attempted inhibition were chloroform, cholesterol and boric acid. Since no measurements were made to determine whether or not actual compound formation took place, we can only say that probably hydrolysis in acid media is not initiated by attack of a proton at the amino nitrogen atom.

The nitrourethan employed in this work was prepared by reacting equivalent quantities of ethylchlorocarbonate and isopropylamine in the

VI SUMMARY

The information recorded in the previous pages may be summarized as follows.

N-Nitrosoacroylmethan has been subjected to hydrolysis in both basic and acidic media, varying the concentration of the hydrolysing agent as well as the time of contact with this reagent.

As a general rule the nitrosoamine is more easily hydrolyzed by acids than by bases, i.e. in a given time interval a given concentration of sodium hydroxide will give a greater degree of hydrolysis than the same concentration of sulfuric acid.

The mechanism of this hydrolytic splitting has been discussed in detail and it was concluded that probably the attack of the acidic and basic reagents takes place at the carbonyl group as in ordinary ester hydrolysis rather than at the amino nitrogen atom as was first postulated for acid hydrolysis.

In order to test the postulated mechanism of acid hydrolysis, certain reagents were to be added to the hydrolysis mixtures in an attempt to form addition compounds, or compounds containing hydrogen bonds with the amino nitrogen atom of the nitrosoamine. In all cases the percentage hydrolysis was the same as that in the absence of a potential inhibitor. The compounds employed in this attempted inhibition were chloroform, cholinerol and boric acid. Since no measurements were made to determine whether or not actual compound formation took place, we can only say that probably hydrolysis in acid media is not initiated by attack of a proton at the amino nitrogen atom.

The nitrosoamine employed in this work was prepared by reacting equivalent quantities of ethylchlorocarbonate and isopropylamine in the

presence of enough sodium hydroxide to take care of all of the hydrogen

chloride evolved.

The nitration was then carried out by adding the urethan to a mix-

ture of fuming nitric acid and acetic anhydride containing a 50% excess of

fuming nitric acid and sufficient acetic anhydride to react with all of the

water in the acid and all of the water formed in the reaction.

The products of hydrolysis were determined to be isopropylnitro-

amine, carbon dioxide and ethyl alcohol. The evolution of carbon dioxide

was employed as the basis for the analytical procedure in the determination

of the degree of hydrolysis in both acidic and basic media. The basic sol-

ution was diluted to volume, aliquots taken, and these aliquots titrated

with standard HCl to the phenolphthalein end-point to neutralize all excess

sodium hydroxide and to the methyl orange end-point to determine the carbon

dioxide evolved. Several runs appeared to give values in the vicinity of

200% hydrolysis until it was realized that the sodium salt of the isopropyl-

nitroamine, which was present in an amount equivalent to the carbon dioxide,

was being titrated simultaneously. Calculations made on this basis gave

logical values for the percentage hydrolysis.

Three methods were employed for collecting the carbon dioxide ev-

olved from the acidic hydrolysis mixtures: adsorption on "Ascarite", absorpt-

ion in barium hydroxide solution and absorption in 35% sodium hydroxide so-

lution. Only the latter method proved to be satisfactory for quantitative

collection of the carbon dioxide. The titrations were carried out as just

described for basic hydrolysis with the exception, of course, that the nitro-

amine did not interfere in the titration.

A yellow impurity which appeared in the sodium hydroxide absorption

tubes was shown to be the sodium salt of nitroform. The nitroform resulted

presence of enough sodium hydroxide to take care of all of the hydrogen

chloride evolved.

The nitration was then carried out by adding the urethan to a mix-

ture of fuming nitric acid and acetic anhydride containing a 50% excess of

fuming nitric acid and sufficient acetic anhydride to react with all of the

water in the acid and all of the water formed in the reaction.

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amine, carbon dioxide and ethyl alcohol. The evolution of carbon dioxide

was employed as the basis for the analytical procedure in the determination

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ution was diluted to volume, aliquots taken, and these aliquots titrated

with standard HCl to the phenolphthalein end-point to neutralize all excess

sodium hydroxide and to the methyl orange end-point to determine the carbon

dioxide evolved. Several runs appeared to give values in the vicinity of

200% hydrolysis until it was realized that the sodium salt of the isopropyl-

nitroamine, which was present in an amount equivalent to the carbon dioxide,

was being titrated simultaneously. Calculations made on this basis gave

logical values for the percentage hydrolysis.

These methods were employed for collecting the carbon dioxide ev-

olved from the acidic hydrolysis mixtures: adsorption on "Ascarite," absorp-

tion in barium hydroxide solution and absorption in 35% sodium hydroxide so-

lution. Only the latter method proved to be satisfactory for quantitative

collection of the carbon dioxide. The titrations were carried out as just

described for basic hydrolysis with the exception, of course, that the nitro-

amine did not interfere in the titration.

A yellow impurity which appeared in the sodium hydroxide absorption

tubes was shown to be the sodium salt of nitroform. The nitroform resulted

from hydrolysis of tetranitromethane present in minute amounts as an impurity in the nitrourethan and was carried over with the carbon dioxide. The tetranitromethane resulted from a reaction between the nitric acid and the acetic anhydride during the nitration of the isopropylurethan.

Isopropylnitroamine was separated from the hydrolysis mixtures by first acidifying them to methyl orange if they were not acid already and then extracting with ether. The ether was removed by distillation on a steam bath and the nitroamine was distilled in a vacuum, boiling point 89°C @ 8 mm.

The substance is acidic and when titrated with standard sodium hydroxide it gave a neutral equivalent of 104, corresponding to the formula $(CH_3)_2-CH-NH(NO_2)$.

Attempts were made to prepare derivatives of isopropylnitroamine. Acidic reagents such as benzoyl chloride and benzenesulfonyl chloride did not appear to react but two basic reagents, morpholine and piperazine, gave satisfactory products.

The morpholine salt had a melting point of 69°-70°C and gave an analysis of 43.77% carbon and 9.12% hydrogen corresponding to a formula $C_7H_{17}N_3O_3$, or one mole of nitroamine per mole of morpholine.

The piperazine salt had a melting point of 114°C and gave an analysis of 40.9% carbon and 9.0% hydrogen corresponding to a formula $C_{10}H_{26}N_6O_4$, or two moles of nitroamine per mole of piperazine.

1. Brühl, Spectrochemistry of Nitrogen, Zeitschrift für physikalishe Chemie, 22, 374 (1897)

2. Chatterway, Tetranitromethane, Journal of The Chemical Society (London), 97, 2100 (1910)

3. Franchimont and Klobbie, Nitrourethans, Recueil des travaux chimiques des Pays-Bas, 7, 343 (1888)

4. Franchimont and Umbgrove, Allylmethylnitroamine, Recueil des travaux chimiques des Pays-Bas, 15, 198 (1896)

5. Franchimont and Van Erp, Contribution to Knowledge of the Nitroamines, Recueil des travaux chimiques des Pays-Bas, 14, 235 (1895)

6. Friedrich, Kühaas, Schnürch; The General Use of the Micro-Kjeldohl Determination, Zeitschrift fur physiologische Chemie, 216, 68-76 (1933)

7. Heinke, The Behavior of Diazomethane Toward Some Nitroamines and Aromatic Nitro Compounds, Berichte der deutschen chemischen Gesellschaft 31, 1395 (1898)

8. Niederl and Niederl, Organic Quantitative Analysis, Wiley & Sons (1940)

9. Pierce and Haenisch, Quantitative Analysis, Second Edition (1940), John Wiley and Sons, New York

10. Shriner and Fuson, Identification of Organic Compounds, Second Edition (1940), John Wiley and Sons, New York

11. Thiele and Lachmann, Nitrourethans, Annalen der Chemie (Justus Liebigs), 288, 291 (1884)

12. Thomas, Propyl and Isopropyl Nitroamine and Derivatives, Recueil des travaux chimiques des Pays-Bas, 9, 69-80 (1890)

13. Umbgrove and Franchimont, Propylnitroamine and Some Derivatives, Recueil des travaux chimiques des Pays-Bas, 17, 270 (1898)

14. Umbgrove and Franchimont, Ethylnitroamine and Derivatives, Recueil des travaux chimiques des Pays-Bas, 16, 385 (1897)

15. Van Erp, The Aliphatic Nitroamines and Nitrourethans, Recueil des travaux chimiques des Pays-Bas, 14, 21 (1895)

16. Watson; Modern Theories of Organic Chemistry, Secton Edition (1941), Oxford University Press, London

17. Zsolonina, N-Nitrobenzenesulfonamides, Journal of The Russian Physical Chemical Society, 31, 645

44.

1. Brühl, Spektropolarimetry of Nitrogen, Zeitschrift für physikalische Chemie, 22, 373 (1897)

2. Chattaway, Tetranitromethane, Journal of the Chemical Society (London), 97, 2100 (1910)

3. Franchimont and Klobule, Nitrourethane, Recueil des travaux chimiques des Pays-Bas, 7, 343 (1888)

4. Franchimont and Thisgrays, Alkylmethylnitrosamine, Recueil des travaux chimiques des Pays-Bas, 15, 199 (1896)

5. Franchimont and Van Dry, Contribution to Knowledge of the Nitrosamines, Recueil des travaux chimiques des Pays-Bas, 14, 255 (1895)

6. Friedrich, Kähnas, Schuster; The General Use of the Meyer-Kielhöhl Determination, Zeitschrift für physiologische Chemie, 216, 68-76 (1933)

7. Reinke, The Behavior of Thiocombhana Toward Some Nitrogenium and Aromatic Nitro Compounds, Berichte der deutschen chemischen Gesellschaft, 31, 1533 (1898)

8. Mladari and Mladari, Organic Quantitative Analysis, Wiley & Sons (1940)

9. Pierce and Haenisch, Quantitative Analysis, Second Edition (1940), John Wiley and Sons, New York

10. Shriner and Fuson, Identification of Organic Compounds, Second Edition (1940), John Wiley and Sons, New York

11. Thiele and Lachmann, Nitrourethane, Annalen der Chemie (Justus Liebigs), 288, 291 (1894)

12. Thomas, Propyl and Isopropyl Nitrosamine and Derivatives, Recueil des travaux chimiques des Pays-Bas, 9, 69-80 (1890)

13. Umbgrove and Franchimont, Propylnitrosamine and Some Derivatives, Recueil des travaux chimiques des Pays-Bas, 16, 370 (1893)

14. Umbgrove and Franchimont, Ethylnitrosamine and Derivatives, Recueil des travaux chimiques des Pays-Bas, 16, 363 (1897)

15. Van Dry, The Aliphatic Nitrosamines and Nitrourethane, Recueil des travaux chimiques des Pays-Bas, 14, 21 (1895)

16. Watson; Modern Theories of Organic Chemistry, Second Edition (1941), Oxford University Press, London

17. Zaolinina, N-Nitrosobenzenesulfonamides, Journal of The Russian Physical Chemical Society, 31, 535